Developing comprehensive and integrated health system reform policies to improve use of medicines

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Colofon

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Chapter 1

General Introduction

Medicines are major contributors to health when used appropriately, and they waste resources and endanger health when overused or used incorrectly. The overall aim of this thesis is to obtain evidence on effective policies to improve use of medicines through impact analysis of the health system reform policies in China. The evidence can hopefully be used by either the Chinese government or other relevant countries to develop or to adjust their health system reform policies more effectively and efficiently in improving use of medicines.

CHINESE HEALTH SYSTEM: STATUS AND TRENDS

Health profile

Mainland China has 31 provincial administrative regions, which include 23 provinces, five autonomous regions, and four municipalities directly under the central government. By the end of 2013, mainland China had a total population of 1.36 billion, of which 630 million (46.3%) lives in rural areas, and 269 million (19.8%) are migrant workers.[1] The main health problems are cancer, heart disease, cerebrovascular disease, respiratory disease, injury and poison, which account for 85.9% of the total deaths. Non-communicable diseases contributed to 82.0 % of the national disease burden.[2,3]

Organization and governance for health

The Chinese health system is organized along four administrative levels: national, provincial, city and county. The state is responsible for overall health policy, while decisions about funding and provision of health services are mainly made at local levels. The state allocates earmarked funding to the poor areas. At the national level, the National Health and Family Planning Commission (NHFPC, formerly named Ministry of Health) is the core agency for health. It is responsible for health legislation, planning and resource allocation, supervising health services and health professionals. The China Food and Drug Administration (CFDA, formerly named State Food and Drug Administration) has the responsibility of supervising the industries of food and medicines. Other ministries also play vital roles in health services and health security, which include the Ministry of Human Resource and Social Security (MoHRSS) and the Ministry of Civil Affairs (MCA). Each local level has its own health, food and medicines, and social security authorities, which are directly administered by the local government and under the technical guidance of respective upper level authorities.

Health financing

Public financing dominated the Chinese health system under a planned economy before the economic reform. All citizens were covered by either the free Government Insurance Scheme (GIS), or Labor Insurance Scheme (LIS), or the Rural Cooperative Medical Scheme (RCMS). After implementing the "opening up" policy in 1978, the rapid economic and technological development led to soaring health expenditures. Meanwhile, the government's health

budget declined, and LIS and RCMS almost collapsed. Financing of health service delivery became increasingly dependent on medicines mark-up (which was allowed by the government as compensation for the declined government subsidy) and out-of-pocket payments. In 2001, the national total health expenditure (THE) accounted 4.6% of GDP. In that year, the share of the government budget for health declined to the lowest level of 15.9% of the total health expenditure, and out-of-pocket health expenditure reached its highest level of 60.0%. The remainder concerned social health expenditures including social and private health insurance, etc.[4]

A new social health insurance system was established in 1998, firstly for the urban employees to replace the LIS. In most areas, GLS was incorporated into the urban employee program, and civil servants were granted with supplementary benefits. The urban employee program is financed by premium contributions from both employers (6% of the employee's wage) and employees (2% of their wage). The retired are exempt from premium contribution. The resident program started with the urban residents in 2007, covering those who are not formally employed. RCMS was re-built in 2003 as the New Cooperative Medical Scheme (NRCMS), and has been integrated with the urban resident program in an increasing number of areas. Both programs are jointly financed by government subsidy and individual contributions. The current social health insurance system consists of the urban employee program and the resident program, which are managed by MoHRSS, and both pool their risks at the municipal level. The NRCMS is managed by NHFPC, with risks pooled at county level. The government also allocates medical assistance funds to subsidize the poor to join either the resident program or the NRCMS, which is managed by MCA. The health security system is jointly financed by the tax-based government health budget, social health insurance contributions, out-of-pocket payments, and private health insurances. NHFPC, MoHRSS and MCA develop the health budget together with the Ministry of Finance (MOF). The risk pool funds reimburse a fixed proportion of health expenditures and limit annual payments to six times the annual average wage of urban employees in the city concerned, and CNY 100,000-200,000 (US$ 17,000-33,000, exchange rate=6) in the county concerned. Expenses exceeding this ceiling are covered by either supplementary insurance schemes or paid by the patient out-of-pocket. Patients with financial difficulties can apply for support by a medical assistance fund from the local agencies of MCA. Local governments are responsible for making up any social risk pool fund deficits. Fee-for-Service is the prevailing provider payment method. Provider payment reforms have been piloted with an aim to shift away from the traditional retrospective fee-for-service (FFS) system to prospective payments, including capitation, global budgets, case-based payments, fixed price per outpatient visit and per inpatient day, etc. Most of the payment initiatives are experimental, and thus have not led to a fundamental change in some providers' perverse financial incentives.[5]

Similar to other products in the pre-economic reform period, prices for medical services and medicinal products are set by the government far below the real cost, aiming to secure the

affordability and accessibility of services and medicines. However, new and highly sophisticated technologies (including brand medicines) are allowed to have high prices. Health service prices of non-profit health providers are set by the local government according to the guidelines developed at the central level, and exempt from tax. For-profit health providers are allowed to set prices for services based on market conditions. Government-owned non-profit health providers receive a government subsidy in exchange for performing social functions of delivering public health and medical services. The quantity and quality of their outputs are determined by the government-specified inputs.

Health service provision

Health services are mainly provided by the public system, which covers 90% of emergency and inpatient services.[6] The historically dual structure of the social and economic development of China led to a split of urban and rural areas, and many rural areas are lagging behind urban areas, also regarding health systems development. Health institutions at different levels have different responsibilities. The urban health delivery system consists of tertiary and secondary hospitals, and of community health centers which are the basis of the health delivery system, and are responsible for curative and rehabilitative services. These services are defined and funded by the government via a "pay-for-performance" approach. Secondary and tertiary hospitals at municipal, provincial and national level support the sustainable development of community health centers by providing technical support, emergency and specialist services, along with carrying out medical education and scientific research.

In the rural areas, the health service delivery system keeps the "three tired structure" which was built in the period of the planned economy. The three tiers are county hospitals, township health centers and village clinics. Township health centers and village clinics mainly provide care for common, prevalent diseases and primary public health services. County hospitals are responsible for acute care and basic health service, and for technical support for township health centers.

Health reform

Recognizing the importance of health as a human right and health sector development as the engine of future economic growth, the Chinese government has launched ambitious reforms to achieve universal health coverage. The target was to ensure universal access to basic health care, as was written in a top-level government document in 2009.[7] Within three years, the coverage of the basic health insurance system and the range of insurance benefits have rapidly increased throughout the country. This is expected to greatly reduce the share of out-of-pocket health expenditures.

Three years after the reform, the government announced to the world that China had achieved universal health coverage for the whole population in 2012.[8] THE raised to over 5.4% of GDP,

the share of government budget for total health expenditures reached a level of 31.3%, and of out-of-pocket health expenditures dropped to 33.4%.[4] Sustained growth in health spending has accompanied China's rapid economic growth over the past decade. Considerable progress in improving health outcomes was reached at the early development stage (1960-1980), when the average yearly GDP growth rate was 5.7% and the average life expectancy increased with 24 years from 43 to 67 years within 20 years. However, improvement of health outcomes got slower after 1980, when China experienced the most rapid economic development (1980-2010). The average GDP growth rate was about 9.9% while the average life expectancy only increased with 7 years from 67 to 74 years within 30 years.[9] During the same period (1980-2010), health progress in China lagged behind countries that had either similar life expectancy levels (Colombia, Malaysia, Mexico, and South Korea, whose average life expectancies had increased with 7–14 years) or had much higher life expectancy figures (Australia, Japan, and Singapore, whose life expectancies increased with 7–10 years during the same period).[10] Life expectancy is expected to increase with one more year between 2011 and 2015, six years after the national health system reform.[11]

Pharmaceuticals

The China Food and Drug Administration (CFDA) is the national regulatory agency in charge of approving new medicines and granting permission for production (active pharmaceutical ingredients, formulations and re-packing) and distribution (wholesalers and retailers). The CFDA is also responsible for providing information about medicines, giving permission to carry out clinical trials, monitoring adverse drug reactions, etc. The authorization is valid for five years and can then be renewed for subsequent five-year periods.

The National Health and Family Planning Commission (NHFPC) plays a role in the formulation of national medicines policy, selection of national essential medicines, and regulation of the use of medicines in health facilities. Secondary and tertiary hospitals are required to set up a Drug and Therapeutics Committee to make recommendations concerning the development of formularies, procurement and stock, and clinical use of medicines.[12] Medicines are reimbursed by the basic health insurance programs together with other health services. Medicines covered by the insurance programs are selected by MoHRSS based on the national essential medicines list but with a broader scope. The maximum retail prices of reimbursed medicines are set by the National Development and Reform Commission (NDRC). Cost-plus pricing was the main method for price setting for a long time, but value-based pricing has been explored more recently. Cost–effective analysis of medicines for pricing and reimbursement decision making is still in an exploring stage. Patients get medicines mainly from health facility pharmacies rather than from retail pharmacies. Medicines stocked by public health facilities are procured by provincial pooled tendering, which is managed by provincial health authorities. Retailers and private health facilities are always run privately as chains, and have their own procurement systems. Buying antimicrobials from retail pharmacies is only possible with a prescription.[13]

There is no formal generic substitution policy at any level in the country. Health facilities are required to stock two strengths for one active ingredient, which are always one cheap generic product and one brand product with higher price. Physicians usually write brand names on the prescription although there is a policy to require generic names for prescription. Both health facility pharmacies and retail pharmacies dispense branded products.[14] Medicines are reimbursed by the basic health insurance programs for a fixed proportion of their cost, no matter whether they are expensive brand off-patent products, less expensive branded generics, or cheap generic generics.

Establishing a secured pharmaceutical supply system on the basis of the national essential medicines system is one key component of the national health system reform. The national essential medicine system is seen as one of the five most important components of the health system reform.[7] A policy for the public health facilities to prescribe essential medicines with "zero-mark-up" has been carried out in urban community health centers across the country since July 2011.[15] The central government formulates and issues the national essential medicines list, and regulates the categories and quantities of essential medicines used at all levels of public health facilities.

The pharmaceutical industry is encouraged and supported by the government with special policies to secure the market supply of essential medicines. Research and development of innovative medicines are highly encouraged by the government, especially biotech products.[16] Modern integrated logistics and chain-store systems for the distribution of medicines are promoted by the government as well.[17]

In conclusion, universal access to essential medicines has generally been secured through universal coverage of the basic health insurance, but a strengthened benefit packages and a more pro-poor perspective are needed to secure more equal access. The "safety net" is to be reinforced to prevent catastrophic pharmaceutical expenditures of the poor families. Perverse incentives in the health systems lead to seriously inappropriate use of medicines in a setting with scarce health resources. This requires innovative and integrated system reforms to remove the perverse incentives and to promote a more evidence-based medicines use.

WHY PERFORMING IMPACT ANALYSIS TO INFORM HEALTH SYSTEM REFORM?

Health system reform is complex and dynamic. Reforms therefore require sound evidence and careful analysis to guide the initial policy development and subsequent policy adjustments, thus increasing the chances of success. Impact analysis is a distinct methodology that is used in the

process of health policy and program formulation and implementation. Such practices can help to identify the causes of poor performance, and may suggest how new policies may improve the design and effectiveness of the policy.[18] Many countries have requested government agencies, independent regulatory agencies, consumer organizations, or other organizations in society to conduct formal and /or informal monitoring and evaluation of new health legislations and health reform policies. Such monitoring and evaluation projects are conducted in different dimensions such as health financing, health service delivery, health technology and products, human resources, governance, information, etc., in order to identify niches for health policy change and gain a better understanding of levers for change. Good examples of this have been well documented by the International Network for Health Policy and Reform, which mainly covers OECD countries. This includes impact evaluation of changes to pharmaceutical benefit scheme pricing on government and consumer medicines expenditures in Australia, an impact evaluation of separating medicines prescribing and dispensing on medicines use in South Korea, etc.[19]

In addition, given the population size and geographic disparity of a country, it is hard for the central government of a country with a large population and huge geographic disparities to implement health system reforms in a uniform way. Most reforms are implemented incrementally, in order to try out new ideas and methods. This enables the government to reduce the risk of making mistakes, and gives time to various stakeholders to adapt to the changes brought about by the reform.[20] The most recent wave of health system reform in China follows such an approach as well. The central government announced broad policy statements and reform strategies, and the local governments are supposed to develop their own implementation plans and to experiment with different models within their local context. Many local innovative health system reforms have therefore been initiated and tested. From time to time, the experiences and lessons are collected to enable rapid learning by key stakeholders, and feedback to the decision-making process. Tracking paths of policy implementation and making timely observation of the policy effects will help policy makers, implementers and regulators to capture the non-linearity and diversity of policy implementation.[21] The success, failure and/or any pre-conditions of local experiments are also valuable for the central government and the other local governments. The information can indicate to the government which new policy could be expanded to broader areas, and under which conditions. This way, good models are identified for promotion and scaling up. National policies and strategies may also change on the basis of feedback from local experiences, which keep changing as a result of learning from pilot projects.[22]

Although the central government invited several international organizations to conduct a review of the most recent wave of health system reforms, there is as yet no well designed and institutionalized mechanism in China to conduct regular policy impact analysis at both central and local levels. In addition, the health system reforms in China are quite extensive and implemented progressively. Few were systematically evaluated. To our knowledge, there are no internationally

published studies which present evidence on the impact of the reforms in sequence, displaying the pathway of reform process from simple and individual policy changes to complex and integrated system reforms. There are only few early appraisals of the reforms internationally published in 2009,[23,24] 2012 (targeting the central level),[25] and 2014 (targeting the local level).[26]

WHY FOCUS THE HEALTH SYSTEM REFOMR IMPACT ANALYSIS ON MEDICINES USE?

Challenges of inappropriate medicines use

Pharmaceutical policies have a significant impact on health system performance. They influence the health of the population, public satisfaction with the health system, the level of out-of-pocket payments and total health expenditures. They also determine the financial burden to both individuals and the public.[27] By 2014, global annual medicines spending reached nearly US$1.0 trillion,[28] and is forecasted to reach nearly US$1.3 trillion by 2018, with an annual growth of about $70 billion (7%) in 2014.[29] Medicines expenditure accounts for as much as 67% of total health expenditures in some countries.[30] At the same time, medicines constitute three of the top ten sources of waste of scarce health resources.[31] Overuse, incorrect use, and disregarding cost-effective use all carry additional costs.

China represents 46% of the "pharmerging" markets, and is already the world's second largest pharmaceutical market, with per capita spending anticipated to grow by over 70% in the next five years. China is now the strategic focal point for many multi-national pharmaceutical companies.[32] Inappropriate use of medicines also brings huge challenges to China. Since the mid-1990's, the national medicines expenditure has always been between 40% and 50% of the national total health expenditure (THE). It was 43.5% in 2006,[33] much higher than that of the median of the low-income countries defined by the World Bank in the same year (29.5%) and twice the level of the global median (23.1%).[34] Thirty to fifty percent of the medicines consumed in hospitals are antimicrobials, around 70% of inpatients are treated with antimicrobials. The consumption of antimicrobials and infusions per capita is far higher that of high income countries (HICs) and the severity of inappropriate use of medicines is even more critical in China than in some low income countries.[35] The consumption of antimicrobials in the primary care is even higher. In 2008, 57% of prescriptions in primary care facilities contained antimicrobials, 39% contained infusions, and the average number of medicines per prescription was 3.1.[36] The levels of these indicators are poorer in China than the global medians obtained by the World Health Organization from a survey conducted in primary care facilities during 1990-2009. These surveys showed a median proportion of prescriptions with antimicrobials of 38.2%, 42.8% and 48.7% in high and upper middle, lower middle, and low income countries, 11%, 15% and 23.2% for infusions, and 2.3, 2.6 and 2.5 for the average number of medicines per prescription.[37] By contrast, when comparing the THE per capita in China with most of the other countries, Chinese patients proportionally spend too much on

medicines. In 2011, the THE per capita in China represents US$ 265 at purchasing power parity, less than the global median (US$ 442) and the global average (US$ 899). It is only one-third of the average in upper middle income countries (US$ 830), and 6% of the average in HICs (US$ 4,246).[38]

Inappropriate use of medicines therefore wastes limited health resources. This brings a huge financial burden to the government, the society, and the individuals, and also carries certain health risks. The number of deaths caused by adverse drug reactions (ADRs) is not known in China. The official data in US mention over 100,000 deaths (0.03%, number of the population of 0.3 billion) caused by ADRs in 1994.[39] On that basis it is not difficult to make a rough estimate of the number of China, which has about five times of the population in US and a more serious misuse of medicines.

In 2005, a study of Public Security Concerns of Irrational Use of Antibiotics[35] estimated that the additional hospital medicines costs due to inappropriate use of antimicrobial is CNY 21.8 billion (US$ 2.7 billion, exchange rate=8.1). The additional hospitalization cost is CNY 42.0 billion (US$ 5.2 billion), the additional medicines costs and hospitalization costs brought by the resistance due to inappropriate use of antimicrobials are CNY 3.7 billion (US $ 0.5 billion) and 1.3 billion (US $ 0.2 billion) respectively. Conducting a multi-factor adjustment, the hospitalization costs of the resistance group is 1.5 times of the sensitive group (non-resistance). With the median hospitalization costs of CNY 7,445.5 (US$ 919) per patient, the additional hospitalization costs brought by resistance can be estimated at CNY 28.9 billion (US $ 3.6 billion,). Based on the actual mortality rate of the patients with resistant bacterial infections (11.7%) and the average mortality rate of general infections (5.4%), the additional deaths brought by the resistance due to inappropriate use of antimicrobials may be around 489,000 per year for the country as a whole. The productivity loss can be estimated at CNY 4.7 billion (US$ 0.6 billion), and the annual medical costs brought by ADRs due to inappropriate use of antimicrobials can be estimated at CNY 1.9-9.1 billion (US$ 0.2-1.1 billion).

Pressure of increasing public funding efficiency

In response to the World Health Organization's advocacy for investments in health, especially aiming for universal access to quality services,[40] an increasing number of emerging economies are now striving toward universal health coverage (UHC). The World Health Report 2013 highlighted the challenge of expanding health services with constant attention to causes of waste and inefficiency that can be reduced through smart policies and wise decisions.[39] In an increasing number of low and middle-income countries (LMIC), the emphasis has shifted from "under funding for health" in the past towards "efficiency and effectiveness of the increased investment in health", following the example of most high income countries (HICs). In addition, providing access to high-cost specialty medicines for prevalent chronic conditions, such as cancers, poses a growing ethical and economic challenge for policy makers at all levels of income.

In the settings where UHC is achieved, and increasingly relying on public funding, efficient use of a defined amount of financial resources is therefore critical for competing with other sectors requesting for public funding. In addition, external pressures from the competing programs also force the insurance to raise efficiency. As a third party payer, health insurance agencies have the leverage to determine types and costs of care they pay for, to negotiate prices of medicines, to dictate quality standards (including better provider prescribing and more cost-effective use), to react to unethical promotion practices, and to demand for supply channel efficiency, etc.[41]

Under the current health system reform, the Chinese government has been continuously increasing its investment in health, aiming to reach universal coverage of the basic health care system. Like in other countries, efficient use of government funding has been increasingly relevant for the success and sustainability of the health system reform. Increasingly, the Chinese Ministry of Finance asks about the efficiency when additional funds for health are requested. Improving the use of medicines plays an important role in this effort, as medicines are one of the major drivers of quality, safety, equity, and cost of care.

In addition, following the achievement of UHC in China, the basic health insurance programs have been the major payers for the medical and medicines expenditures. In 2011, the total expenditure of the basic health insurance programs was CNY 654.1 billion (US$ 104, exchange rate=6.3), accounting for half of the total health facility revenues. In some areas, this share has reached 80%-90%.[9,42,43] With the increasing financial pressure of improving the benefit package (including continuously increased payment by insurance, covering more and more high-cost medicines and other high-tech health interventions), the basic health insurance programs have been adopting more initiatives to contain cost, including the cost of medicines.

Need of effective policies to improve medicines use with health system perspective

A major step towards improving use of medicines was taken in Nairobi in 1985 at an international conference,[44] when an action plan to improve the use of medicines worldwide was discussed, and later adopted by the 1986 World Health Assembly. This triggered a series of actions to improve the use of medicines that are still relevant today: international guidelines to develop national medicines policies, programs to strengthen regulatory authorities, teaching materials for health care professionals, good procurement and distribution practices, and global standards for information about medicines, etc. Following these recommendations, World Health Organization also urged Member States to "consider establishing and/or strengthening a dedicated national programme and/or multidisciplinary national body, guided by a broad-based, long-term, independent steering committee, involving civil society and professional bodies, to monitor and promote appropriate use of medicines.[45,46] Twelve core interventions are recommended by the World Health Organization to promote quality use of medicines, in which "avoidance of perverse financial incentives" and "multi-disciplinary activities" are emphasized. Several key blocks of the

health system-leadership and governance, financing and information are highlighted in addition to the traditional clinical approaches like guidelines and essential medicines list.[47] Addressing the problems of medicines use with a health system perspective has been increasingly stressed globally.

To promote the appropriate use of medicines, the Chinese government introduced and implemented a series of regulations and strategies. However, in general their effects on improving the use of medicines were limited. These policies and regulations included requests to retail pharmacies to sell antimicrobials only with prescriptions in 2003,[48] and developing clinical pathways, standard treatment guidelines and clinical use guideline of antibiotics and other medicines in 2004.[49] A national antimicrobials clinical use and resistance monitoring network was created in 2005 to collect, analyze and report routine data from tertiary hospitals.[50] Prescriptions were formally regulated in 2007,[14] and pharmacy administration in health facilities was further strengthened in 2011.[12] A national medicines use monitoring network was set up in 2009 to collect medicines use data from the secondary health facilities, and to recommend interventions for improving medicines use.[51] The types of antimicrobials to be stocked and used in different levels of health facilities were clearly defined and national targets of antimicrobial clinical use were set in 2012.[52]

Although there have been numerous policies issued for improving medicines use during the past ten years, and national medicines use monitoring networks and a national expert committee for quality use of medicines have been in place for some time, the problem of inappropriate use of medicines remains fundamentally unresolved. In 2010, the proportion of national pharmaceutical expenditure to the total national health expenditure was still 40.3%,[38] with the average proportion of outpatient and inpatient medicines cost still at 50.7% and 43.4% of expenditure of public hospitals.[53] This is an unacceptably high level. Among the top 20 adverse drug reaction reports of allopathic ("Western") medicines in 2010, 15 are from anti-infectious medicines; the top-three are levofloxacin, azithromycin, and ceftriaxone; 73.6% of the adverse drug event reports are infusions,[54] indicating the severity of inappropriate use of infusions (often with antibiotics).

The main reason for the lack of success in improving prescribing is that intervention strategies have remained limited to executive orders and one-time inspections within the scope of clinical educational interventions. The pharmaceutical sector is a complex sector, with many stakeholders and different interests involved. Policy interventions on medicines use by any one actor will impact the behavior of others. Because of the special nature of the sector, a case-by-case solution targeting an individual problem often fails to achieve the expected result, as the goals of individual policies may be somewhat inconsistent or even mutually conflicting. Moreover, the interests of different entities often interfere with each other. Fragmented and vertical approaches rather than integrated strategies with health system perspective, a lack

of association between clinical and social sciences, or neglecting the behavior characteristics of prescriber and patients, will never solve the problem of inappropriate use effectively and sustainably.

In addition, the Chinese health system still suffers from perverse financial incentives, which also promote the inappropriate use of medicines. These perverse incentives include government subsidy approaches (limited resources focus on tertiary hospitals and infrastructure constructions), distorting pricing policies (the level of medical service price is far below the real cost, while the levels of large scale medical equipment diagnosis, medical supplies and medicines are much higher than the real cost), and the revenue of medicines sales is used as a major source of financing for public health facilities. Additional problems are insufficient public resources for a "fee-for-service" payment mechanism, unsound medicines procurement mechanisms without appropriate incentives for facilities to procure low-priced medicines, and a "reversed-proof" responsibility for medical disputes which encourages a defensive, high-prescription attitude of doctors.

These perverse incentives distort the behaviors of health professionals and intensify inappropriate use of medicines. A wider health systems approach is needed to achieve long term, equitable and sustainable results. The global movement toward universal coverage has the potential to create necessary incentives for both providers and patients in changing their behaviors of using medicines. It is urgent to explore the relationships between such behaviors and health financing mechanisms.

There is an opportunity for the national health system reform to address these perverse incentives. The top decision makers are clearly committed to change medicines revenue as a major source of financing for health facilities, and have required health insurance programs to develop innovative strategies to create other incentives for appropriate use of medicines. These measures include expanding coverage to both inpatient and outpatient services; increased diagnosis, treatment and dispensing fees to make up for the loss of medicine sales revenue; changing payment methods from retrospective fee-for-service to prospective capitation-based payments; and supporting polices to secure the quality of care, including the appropriate use of medicines.

In summary, given the importance of informing the health system reforms through impact analysis, and considering the critical role of pharmaceuticals in the reforms and the huge challenges of inappropriate use of medicines, it is essential to perform a systematic impact analysis of health system reforms on medicines use in China. However, previous reviews have shown the lack of systematic scientific studies to evaluate the effects of pharmaceutical policies and strategies in low and middle income countries.[56-57] Systematic formal evaluation of new

medicines policies has not yet been established in China.[58] The studies included in this thesis therefore respond to the increasing need of informed health and pharmaceutical policy. They assess several components of the health system reforms[59] and cover both the intended and unintended effects of the reform policies.[60,61]

OBJECTIVE AND RESEARCH QUESTIONS

The objective of this thesis is to obtain evidence on developing effective policies to improve medicines use in China, through an analysis of the impact of health system reform. The thesis describes the status and trends of Chinese health system; analyzes the challenges of the Chinese pharmaceutical system; elaborates the rationale for making an impact analysis of various components of health system reform policies on medicines; measures the effect of clinical educational interventions and financing reforms to promote appropriate use of medicines over the period of 2008-2012; and measures the effects of integrated system reforms on the use of health services and medicines. The thesis ends with an analysis of the possible policy implications for the Chinese government, which may also be relevant for other governments engaged in similar system reforms.

The specific research questions addressed in this thesis are:

1. What are the general strengths and challenges of the Chinese pharmaceutical system?
2. What are the effects of clinical educational interventions on medicines use, with a focus on antibiotics?
3. What are the effects of various financing reforms on the use of health services and medicines within the health system reform framework?
4. What are the effects of integrated system reforms on the use of health services and medicines within the health system reform framework?

OUTLINE OF THE THESIS

This thesis consists of eight studies, divided over four chapters. Following the **General Introduction** in **Chapter 1**, **Chapter 2** sets the scene of the overall situation of pharmaceuticals and medicines use in China. **Chapter 2.1** describes and examines the main problems existing in the whole chain of provision of pharmaceuticals, from registration, production, distribution, to utilization and administration, and analyzes the main socio-economic and institutional factors associated with these key problems. The paper ends with several policy recommendations to the government in tackling the problems and addressing the challenges of developing a healthy pharmaceutical sector. **Chapter 2.2** reports on measuring the availability and use of essential medicines in two provinces of China just at the time when the most recent wave of health system reform was launched in 2009. The results can be regarded as a baseline measurement for the

national health system reform. The discussions in this study intend to identify strategies to improve affordable access to essential medicines under the reform.

Chapter 3 describes clinical educational interventions on antibiotic use and the effects of these interventions. **Chapter 3.1** focuses on antibiotic prophylaxis in Chinese hospitals, reporting on a systematic review of intervention studies on antibiotic prophylaxis in clean or clean-contaminated surgery in Chinese hospitals from 2000 to 2012. **Chapter 3.2** concerns the Plan of Action for Sino-Swedish Health Cooperation 2011-2014 of the Sino-Swedish Working Group on Antibiotic Resistance. This plan aims to apply Swedish expertise to antibiotic resistance containment in China. The study analyzes changes in the patterns of antibiotic use in Chinese hospitals, and compares these with Chinese national targets and with antibiotic use in Swedish hospitals.

Chapter 4 includes two studies on the effects of the"medicines zero mark-up policy" which aims to remove the reliance of providers on medicines sales, and “provider payment reform” which intends to shift from retrospective payment to cost sensitive prospective payment. These two studies target the most important financial components of the health system reforms, which aim to remove the perverse incentives for medicines overuse and cost escalation, and to create a positive incentive for cost-effective use and cost awareness. The studies both focus on primary care where the two reform components were initiated, one in urban area, and the other in a rural area. **Chapter 4.1** reports on the effect of implementing three different health care financing mechanisms in Beijing community health facilities in parallel with the introduction of "medicines zero mark-up policy". This study analyzes the cost containment effect and its effect on the operation of community health facilities. **Chapter 4.2** reports on the effect of shifting the provider payment from a fee-for-service system to capitation payment in Qianjiang (a less developed county in western China). The NRCMS of Qianjiang regarded the provider payment as a tool to contain cost escalation and to change prescription behaviors at the beginning of the reform. Key measurements included cost, prescription behaviour, hospitalization and referral rate, and provider income.

Chapter 5 records the initiatives of one special economic development area (zhuhai) in developing integrated health system policies to improve medicines use. **Chapter 5.1** documents local experiences in designing and improving the basic health insurance system from the dimensions of population coverage, service coverage and financial risk protection. This paper describes the development of Zhuhai’s basic health insurance system chronologically. It analyzes the background and the key components of the common disease outpatient benefit package, and makes a comparison with outpatient benefit packages of other areas of China and four neighboring countries. **Chapter 5.2** presents the first study in China in which routine data from various sources were systematically collected and analysed to assess the effect of a local health insurance reform programme. Longitudinal data from the health insurance organizations, the

health administrative bureau, and primary care facilities were used to assess trajectories in outpatient visits, inpatient admissions, cost per common disease outpatient visit, and prescribing indicators over time. The results highlight the fact that existing data from different sources can be used to inform health policy.

In **Chapter 6**, a general discussion reviews the results of the studies in the light of the research questions and identifies some lessons learnt. It also reviews the possible practical implications of the research outcomes and formulates a number of practical recommendations for further promoting universal access to basic health care, in a cost-effective and sustainable way. Some methodological challenges for policy impact analysis are also identified and discussed. **An executive summary** in English, Netherlands and Chinese is presented in the end of the thesis.

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Chapter 2

Setting the Scene: the Pharmaceutical Sector and Medicines Use

2.1 Pharmaceutical Policy in China: Issues and Problems–Background Paper for the Study on China´s Health System Reform

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Report prepared for the Chinese government for the national health system reform
WHO Archive

ABSTRACT

This policy review comprehensively examines China's pharmaceutical policy, covering the whole pharmaceutical sector, from medicines registration, production, distribution, to medicines utilization and administration. The aim of this paper is to describe and examine main problems existing in the pharmaceutical sector, and to analyze the socio-economic and institutional factors associated with these key problems. The paper ends with several policy recommendations that can be adopted by the Chinese government to tackle the problems and to address the challenges in developing a healthy pharmaceutical sector.

INTRODUCTION

Since its launch of the economic reform in late 1970s, China's economy has developed rapidly. The annual growth rate of GDP has been maintained at an average level of 14% over the past two decades.[1] Living standards of vast majority of the Chinese population have increased significantly, and over 550 million people have been moved out of the poverty. However, access to basic health care of most Chinese population has not been improved in a way that matches its economic growth. The problem has particularly become serious for the poor, owing largely to a rapid rise of medical care costs and lack of health insurance coverage.[2] In addition the quality of care also varies greatly among different service providers and in different areas.

The national health account studies show that China spent 4.7% of GDP on health care in 2004, of which 44% was on pharmaceuticals. Such a share of pharmaceutical expenditure is high in the world, compared to an average of around 15% in the OECD countries.[3] Patients in China tend to be treated in a costly way, and in some cases, the extra cost are not warranted from a medical perspective. Overuse of medicines is a well-known problem in Chinese hospitals, since pharmaceutical sale have been a key part of the revenue in general, and also a major contributor to bonus of doctors.[4,5] In other words, the more medicines doctors prescribe, the higher income they can earn. Such a perverse financial incentive has huge implications for quality and cost of health care. One study found that only less than one percentage of medicine prescriptions was actually reasonable in the studied village clinics.[6] Over-prescription has also placed an unnecessary financial burden on many poor families not covered by health insurance.

Over the past two decades, China's pharmaceutical industry has also been greatly developed. More than 4,600 pharmaceutical manufacturers, 12,000 wholesalers and 270,000 retailers, produce and sell more than ten thousand western and traditional Chinese medicines. Both central and local governments have seen pharmaceutical industry as one of key economic sectors driving robust development of the economy. These manufacturers are producing mainly generics and/or traditional Chinese medicines. However, some cheap and less profitable essential medicines are no longer produced and available on the market.

Over the past decade, there have been many studies in China looking at the use of medicines and its socio-economic affecting factors.[4,7] However, few international publications have comprehensively examined China's pharmaceutical policy covering the whole process of pharmaceutical registration, production, distribution, and utilization and administration. Against this background, this paper aims to describe and examine the main problems existed in the Chinese pharmaceutical sector, and to analyze the socio-economic and institutional factors associated with these key problems. The paper ends with several policy recommendations that can be adopted by the Chinese government to address the problems and challenges for developing a healthy pharmaceutical system.

ECONOMIC REFORM AND IMPLICATIONS FOR THE PHARMACEUTICAL SECTOR IN CHINA

The economic reform has led to a transformation of China from a planned economy to a market oriented one. The government funding to health facilities has become less important since mid 1980s, representing the decreasing ratio of government budget to total hospital revenue. Health facilities have increasingly relied on service fees from users who may or may not be covered by health insurance. Supplying more diagnostic tests and medicines is one of the key means to cover the operational cost, and to increase the income of health professionals via legal or illegal methods (bonus payment, medicines sales commissions and kickbacks). Using fee-for-service as a main provider payment method has been worsening the situation. As a result, the health expenditure has risen rapidly. The average annual growth rate of the total health expenditure in China was up to 18.2% over the period of 1991-2004, while the average growth rate of GDP was only 9.3% and the average GDP per capita growth rate was 8.2% in the same period.[8]

China has kept low prices for most health services through government regulation. The prices are not set based on cost, except for medicines and "new" high-technology services. For which, the price can be set at a higher level than actual cost, to allow for a profit margin. Chinese hospitals are allowed to mark up medicines by 15-20% above the wholesale price (30% for Chinese herbs).[9] In addition, the use of fee-for-service, as a major provider payment method also significantly contributed to the supply-induced demand. According to one study,[10] it has contributed from 85.5% to 90.3% of the total health expenditure in two relatively well-off Chinese counties in 1992.

China's economic reform has also brought a good opportunity for pharmaceutical industry to develop in an impressive way. In early 1980s, there were only 839 pharmaceutical manufacturers in China, producing around 1,200 western medicines. In addition, there were about 540 traditional Chinese medicine manufacturers producing about 600 traditional Chinese medicines. The number rose remarkably to over 4,600 western pharmaceutical manufacturers in 2005. Only 3,731 of them got GMP certificate in 2004. The total pharmaceutical product value increased from CNY 10 billion (US$ 3.1 billion, exchange rate=3.2) in 1985 to over CNY 446 billion (US$ 55 billion, exchange rate=8.1) in 2005.[11] The pharmaceutical industry has played an important role in developing local economies and creating jobs for local government. Nevertheless, China has too many small/middle-size pharmaceutical manufacturers, most of which can only produce generics and/or traditional Chinese medicines.

Pharmaceutical policy

Prior to the economic reform in China, the government was responsible for making a production plan of pharmaceuticals (e.g. types and quantity of medicines) for all the state-owned pharmaceutical manufacturers. Likewise, the government also established a network

for the supply and distribution of all pharmaceuticals. Under this system, the state-owned pharmaceutical distributors and companies at different levels were responsible to sell medicines to health facilities across the country. At that time, manufacturers were not allowed to sell products directly to health facilities.

After the economic reform, new regulations and decrees regarding the production and distribution of medicines were developed to help introducing more market mechanisms into the state-owned pharmaceutical manufacturers, in order to promote the development of the pharmaceutical industry. In September 1984, "The Drug Administration Law" was issued, aimed to ensure the quality, safety and efficacy of medicines under the context of transforming China's planned pharmaceutical sector into a market-oriented one. Since 1990s, an increasing number of issues and problems related to pharmaceutical production, registration, distribution, and utilization emerged. The following three sections are devoted to illustrate what the main problems, how serious they are, and what factors they are associated with.

Pharmaceutical registration, production and pricing

Under the market-oriented economy, Chinese pharmaceutical manufacturers have the autonomy to decide what products and how much they would produce. It is not surprising that manufacturers develop their production plans according to market demands and profit gains, although the production of some special medicines is still strictly regulated by the government. The State Food and Drug Administration (SFDA) is responsible for reviewing and approving new medicines on the ground of quality, safety and efficacy. The National Development and Reform Commission (NDRC) is mandated to set and regulate the prices of new medicines based on self-reported production costs suggested by the manufacturers. Prices of medicines listed by the national health insurance programs are also set by NDRC.

As described above, health expenditure in China has increased significantly since the economic reform. Over the past two decades, it was the individuals, not the government, who have mainly born the financial burden emanating from the rapid rise of medical care costs. Part of increased spending was contributed by the advanced health technologies that have brought higher quality of care, but some of the increased expense was just caused by over-use of medicines and diagnostic tests. Many studies found that there were an increasing number of people who were unable to get access to basic health care. The equity in access to and financing of health care were worsening.[12] In order to reduce the financial burden of medicines expenditure, there were 20 rounds of medicines price cutting since 1997. The prices of a number of selected medicines (mostly were essential medicines) were cut down significantly. However, patients did benefit from the price cuttings. Pharmaceutical manufacturers stopped producing the products which were subject to price cutting, and shifted to other products. A study found that,[13] one third of 1,500 essential medicines was out-off-stock in Beijing, and 30% of which were no longer produced

by any Chinese pharmaceutical manufacturers. Such a phenomenon is common in other areas as well.

Pharmaceutical manufacturers are keen to register "new products" to evade price cutting for more profits. The "new products" are unfortunately non-innovative, just modifications of dosages and/or packaging, but are not subject to price cutting any more. Until the end of August 2006, SFDA granted 176,000 medicine approvals,[a] among which the majorities are new dosages and/or packages. For example, until the end of February 2007, SFDA issued more than 200 approvals of Levofloxacin injection.[14] On the contrary, no manufacturers would be willing to produce less profitable product like Vitamin D2. It was replaced by two activated Vitamin D (Alfacalcidol and Calcitriol). As a result, the daily treatment cost rose from less than CNY 1 to 10-15 (US$ 0.1 to 1.4-2.1, exchange rate=7.3).

Another important factor that has been affecting the production of medicines in China is the medicines lists developed by different health insurance schemes. Although the national essential medicines list was already developed by MoH in responding to the World Health Organization's Action Program for Essential Medicines, it has not really influenced on the production and use of medicines in China due to the lack of relevant policy support. Instead, medicines list developed by the insurance programs play a key role in guiding the production. The Ministry of Labor and Social Security (MoLSS) develops the reimbursable medicines list for the urban employee basic medical insurance (BMI). It consists of 1,901 medicines, of which 823 are traditional Chinese medicines. Rural co-operative medical scheme (RCMS) is managed at county level, and each county may have its own medicines list for reimbursement.

The quality of locally produced medicines in China has been improved gradually during the past decade since the reinforcement of the national drug regulatory authority in 1998. However, given such a huge number of pharmaceutical manufacturers, the supervision capacity may not be adequate enough for appropriate overseas. Quality issue and even counterfeit medicines emerged outstandingly. Counterfeit medicines are global public health problems causing death, disability and injury to adults and children, which plague both developing and developed countries. Developed countries with effective regulatory systems and market control always keep a low market value (less than 1%) of counterfeit medicines. While in countries where there is weak regulatory function, 10-30% of medicines on sale can be counterfeit.[15] In China, 332,000 cases of counterfeit medicines and medical devices were investigated in the distribution chain in 2006, which were worth about CNY 0.6 billion (US$ 73 million, exchange rate=7.8); four manufacturers were revoked of the production licenses and 142 were requested to stop

[a]One medicine product may have a number of registration numbers approved by the SFDA for different manufacturers, different dosages and/or package, etc.

production; 160 distributors were revoked of the distribution licenses and 114 were shutout; 86 GMP certificates and 135 GSP certificates were withdrew; 440 counterfeit medicines production venues were eradicated.[16] Some new characteristics of counterfeit medicines cases in China are seen as increased cases in R&D process, submission of fake dossiers, non-compliance of standard operation procedures in production process; distorted distribution system, etc.

Strong government regulation in the pharmaceutical chain is essential to safeguard the population against counterfeit medicines. Meanwhile, it also makes this sector particularly prone to corruption. If the drug regulatory authority enjoys un-supervised and un-checked power, loopholes would definitely arise. A chaotic registration process for new medicines and medical devices has been reported as a major cause for the rapid increase of medicine prices in China. Bribery paves the way for easy registration of so called "new products" to evade price regulation.

Pharmaceutical distribution

There have been significant changes in pharmaceutical distribution systems since the economic reform. As said above, the government previously organized a network for the supply and distribution of all medicines made by Chinese manufacturers. Prior to the reform, the state-owned wholesalers were responsible for purchasing medicines from manufacturers. Three levels of medicines wholesalers (province, prefecture and county) had been established to supply pharmaceuticals to hospitals at respective levels. Dong[9] described a clear flow of distribution of medicines in China within the old system. The advantages of this distribution network were to have effective control and monitoring of medicines quality and price. Dis-advantages as pointed by Dong were the lack of competition and bureaucratic procedures, which might associate with poor management and storage.

After the reform, both distributors and manufacturers are allowed to sell medicines directly to hospitals and pharmacies. In other words, each of the 4,600 pharmaceutical manufacturers can also act as distributor. Most distributors are with small size. It appears to have too many distributors in the pharmaceutical distribution system, which is not easy to be well regulated.

Most pharmaceutical manufacturers have been actively promoting their products, using a variety of ways including sending medical representatives to promote prescriptions in hospitals. Commissions, kickbacks, or gifts are given to hospital managers and/or doctors who purchased or prescribed their products. Senior doctors are supported by pharmaceutical companies to participate in international conferences as a reward of prescription. Such activities have greatly influenced prescription behaviors. The financial incentives given by the manufacturers to hospitals and doctors might have resulted in purchasing less effective but expensive medicines, inappropriate prescriptions and poly-pharmacy. In addition, advertising has also affected the choice of medicines by both service providers and users, as found in other countries.[17]

The number of retail pharmacies across the country also increased greatly over the past two decades after the introduction of the market economy. In 2006, 270,000 retail pharmacies were registered with the drug regulatory authority.[14] This enabled conveniences of access to medicines of the Chinese population in both urban and rural areas. According to the national health account study, about 20% of medicines expenditure was associated with retail pharmacies. Although regulations on controlling the distribution system have been put in place, the implementation is still problematic, especially at low levels. In practice, most rural retail pharmacies, particularly at the county and township levels, often do not have any technical supports from qualified pharmacists. This has huge implications of the quality and safety of care.

In 2004, SFDA issued a regulation requiring that antimicrobials cannot be purchased without prescription in retail pharmacies. Such a policy aimed to improve medicines use (e.g. prevent the over-use of antibiotics).[18] In fact, only a few number of pharmacies have well followed up the regulation. In most pharmacies, particularly in the rural areas, patients can still buy various antibiotics without a prescription. Lacking of capacity for monitoring and supervision on such a large number of pharmacies led to a failure of effective implementation of this regulation.

Appropriate use of medicines

Inappropriate use of medicines is a major problem worldwide. World Health Organization estimates that more than half of all medicines are prescribed, dispensed, or sold inappropriately, and that half of all patients fail to take them correctly.[19] Overuse, under use, or misuse of medicines has resulted in wastage of scarce resources, poor quality and unnecessary costs of health care.

Inappropriate use of medicines is also a serious problem in China. Many studies demonstrated inappropriate use in different health facilities at different levels since early 1990s.[4,7] Common problems include too many medicines given in one prescription; inappropriate use of antibiotics and steroids, abuse of intravenous drip. In 2005, a prescription inspection was conducted in seven secondary and tertiary hospitals in Zhuhai area. The result showed that 58% of outpatient services were prescribed with injectables. Over 80% of prescriptions of the Departments of Pediatrics, Respiration Internal Medicine and Surgery used antibacterial injectables.[20] The main factors attributed to these mal-practices in medicines use include 1) perverse financial incentive; 2) lack of clear official guidelines and corresponding review for treatment of common diseases; and 3) lack of knowledge of doctors or pharmacists at the grassroots level.

The national essential medicines list has not been influential to the prescribing behavior. Instead, the medicines lists developed by insurance programs have had greater impact on doctor's prescribing behaviors and patient choices.[21] Cheap and effective essential medicines may not

be included in the reimbursement lists. Sometimes this is because of adverse events due to inappropriate use of some first line medicines (e.g. persisting use of gentamycin with a large dosage for a long time, especially intravenous injectables, led to deafness of many children). The health authority then decided not to recommend the use of these medicines. In fact, if these medicines had appropriately been used, such negative consequences would have been avoided in most cases.

RECOMMENDATIONS TO ADDRESS THE CHALLENGES

The above section has described and analyzed main problems associated with pharmaceutical registration, production, distribution and appropriate use. Apparently, many issues and problems need to be adequately addressed in order to establish an effective and efficient pharmaceutical sector in China in the near future. Given the limited space of the paper, this section will focus its main attention to the following issues.

Developing appropriate National Medicines Policy

The pharmaceutical sector is complex. Many stakeholders and different interests are involved in pharmaceutical sector. A case-by-case solution targeting an individual problem often fails to achieve the expected results. The goals of individual policies may be somewhat in-consistent or even mutually conflicting. Moreover, the interests of different entities often interfere with each other. Therefore, many countries have chosen to develop national medicines policy (NMP) in order to integrate policies across different areas of the pharmaceutical sector, and to guide the whole process of medicines research and development, production, distribution and utilization.

Given the current situation in China and the problems in its pharmaceutical sector, it is urgently needed and highly desirable to set up a comprehensive NMP, which can consolidate individual policies, and give clear direction for the development of pharmaceutical sector to serve the health and well being of the people. It can define and record national objectives in the pharmaceutical sector, address problems in an integrated way, set national priorities and strategies, and guide different stakeholders work in a collaborative way. Based on this general policy, concrete policies in specific fields can be adjusted and refined.

The government needs to develop a balanced policy in promoting both the development of pharmaceutical industry and access to essential medicines. Under the auspices of the State Council, the National Development and Reform Commission, the Ministry of Finance, together with the Ministry of Health and the Ministry of Labor and Social Security, need to work together to develop effective and adequate regulations on essential medicines pricing, distribution and procurement.

Pharmaceutical sector has been regarded as one of the key economic pillars to push a fast growth of local economy. A rapid development of pharmaceutical sector can be good for the growth of GDP, an important indicator used for the performance assessment of local politicians. It is not surprising to see that in the 11th Five Year Plan, indicators related to the total product values of the pharmaceutical sector and the jobs associated with the sector were included. As a result of such policies coupled with the economic transition, there have been an increasing number of pharmaceutical manufacturers set up across the country. Most are small or middle size, and cannot reach an optimal economy of scale.

Needless to say, the development of pharmaceutical sector has significantly contributed to the economy and employment and improved the availability of medicines in many regions of China. However, vigorous development without appropriate plan always led to vicious competition. In some provinces, this has been one of the main factors indirectly push a rapid escalation of health care costs over the past decades. Such a situation might have also been indirectly associated with the poor affordability and accessibility of health care by a majority of the Chinese population in recent years. This implies that senior politicians and policy-makers at both national and regional levels need to rethink the necessity and importance of rebalancing the economic development with the health objectives.

However, if the perverse incentives (hospital revenues rely on medicines sales) are not removed, even if the NMP is formulated, the problem of inappropriate use will remain. Actions are needed to strengthen the drug regulatory and supervision functions, to reform the distorted pricing system, to change the provider payment, etc., in order to create appropriate incentives for producing and appropriate use of quality essential medicines.

Strengthening registration, production and pricing of medicines

Regulation on medicines registration, production and distribution should be stricter and more robust under the guidance of clear national goals and objectives for the pharmaceutical sector. The capacity of the drug regulatory authorities should be further strengthened to secure better enforcement of laws and regulations. Twenty times of price cutting has not been helpful in addressing the escalation of medicines expenditure and the issue of affordability of essential medicines. To encourage the production of cheap and effective essential medicines, appropriate incentives should be granted to the manufacturers. Better coordination between the health insurance programs and the pricing authority is needed to secure that reimbursed medicines are cost-effective.

Creating appropriate incentives for appropriate use of medicines

The health financing mechanisms need to be reformed to remove the perverse incentives and to create positive incentives for appropriate use of medicines. De-linking the income of doctors with the revenue generated from medicines sale is vital for this. In recent years, several

experimental studies in different areas have demonstrated this.[22,23] With the support from DFID, UK and the Government of China, four Chinese cities (Chengdu, Shenyang, Yinchuan and Xining) have developed effective community health service system aiming to provide affordable and effective basic health care to the urban residents. Doctors working in these community health facilities have been paid salary and bonus. The later payment is linked with his/her performance assessment, instead of revenue generation. Apparently, use of medicines in these centers has been more rationalized after the separation of income from revenue generation. Another example is the community health centers of Changning District, Shanghai where the district government and the urban BMI scheme use global budget, plus indicators (e.g. capped expenditure per outpatient visit), to purchase public health/preventive services and essential clinical services, respectively. Doctor's income is no longer associated with their revenue generation. The impact of such a reform is clear. The average expenditure per outpatient visit declined 25%-10.7% in 2006 comparing with that in 2005.[24]

With such a pre-condition that perverse incentives are removed, traditional clinical based approaches will be more effective in promoting quality use of medicines.[25] As far as possible, treatment should be evidence-based and accounting local economic realities. Standard Treatment Guideline (STG) should be officially launched by the government following with intensive trainings at all levels of use around the country, and periodically updated based on the comments from the grassroots.[26] Essential Medicines List (EML) and formularies could be used as another useful tool to promote quality use of medicines. It has been generally accepted that the selection of medicines should be based on a list of common conditions and the treatments of choice for these conditions are as defined in STGs.[27] Drug and Therapeutics Committee in hospitals should play an important role at grass root level in promoting appropriate use of medicines.

Evidence–based policy making

Before any reform decisions making, at least an effort should be made to describe and quantify the problems. An indicator-based assessment should be followed by more detailed studies on individual medicines or specific diseases, and the availability/affordability of essential medicines. A time-series of such surveys is extremely useful to monitor the performance with defined targets, and this can also serve as a baseline for the planned interventions.[28] Decision makers will benefit from getting these quantitative data to understand accurately the major problems, which could help to make appropriate reform policies.

CONCLUSION

The pharmaceutical sector of China experienced a rapid development following the economic reform. Emerging issues of medicines R&D, registration, pricing, distribution and clinical use in the new market economy environment are to be addressed with more rigorous and

effective regulation policies and strategies. It is critical to remove the perverse incentives in the health systems to create a clear policy environment for promotion of quality use. Developing appropriate National Medicines Policy to balance the economic development with the health objective is essential for a healthy pharmaceutical development. Strengthening medicines registration, production and pricing, creating appropriate incentives for appropriate use of medicines, and promoting evidence-based policy making are the pressing actions for the government at this stage.

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Chapter 2

Setting the Scene: the Pharmaceutical Sector and Medicines Use

2.2 Availability and Use of Essential Medicines in China: Manufacturing, Supply, and Prescribing in Shandongand Gansu Provinces

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ABSTRACT

The current health system reform in China launched in 2009 tackles the problem of access to appropriate medicines for its 1.3 billion people by focusing on providing essential medicines to all. To provide evidence for the reform process, we investigated the manufacturing, procurement, and prescribing of essential medicines in two provinces. We conducted surveys in 2007 of all manufacturers (n=253) and of 59 purposively selected retail pharmacies and 63 hospital pharmacies in Shandong and Gansu provinces. The production and supply of essential medicines, as well as factors underlying decision making about the production and supply were assessed. We also reviewed prescriptions (n=5,456) in health facilities to assess the use of medicines. Overall, manufacturers in Shandong and Gansu produced only 62% and 50%, respectively, of the essential medicines they were licensed to produce. Of a randomly selected 10% of essential medicines, retail pharmacies stocked up to 60% of western products. The median availability in hospital pharmacies ranged from 19% to 69%. Manufacturer and retail pharmacy managers made decisions of medicines production and stock on economic considerations, while hospital pharmacy managers cited clinical need. Between 64% and 86% of prescriptions contained at least one essential medicines. However, over prescribing of antibiotics (34%-77% of prescriptions) and injectables (22%-61%) for adult non-infectious outpatient consultations was common. We found that manufacturers, retail pharmacies, and hospital pharmacies paid limited attention to China's 2004 national essential medicines list (NEML) in the decisions of manufacturing, procurement and stock of essential medicines. We also found that prescribing of essential medicines was frequently inappropriate. These results should inform strategies to improve affordable access to essential medicines under the current health system reform.

BACKGROUND

China spent 4.5% of Gross Domestic Product (GDP) on health care in 2007. Although total health expenditures have been modest relative to GDP, pharmaceutical expenditures account for a significant proportion, averaging over 40% in the past two decades.[1] In contrast, the average percentage in OECD countries was around 15%.[2]

Despite high pharmaceutical spending, China experiences substantial problems in access to medicines, due to both the lack of availability of essential medicines and to the high cost of and preference for branded products.[3] Perverse financial incentives to service providers lie at the core of these problems. A large proportion of hospital revenue comes from profits from pharmaceutical sales, often the most important source of income at county and lower level hospitals and health centers.[4,5] Service providers make greater profits on higher priced pharmaceuticals, since the mark-up rate is fixed by government regulation. Hence, Chinese doctors tend to over prescribe medicines, in particular expensive medicines, to maximize revenue generation for their institutions and bonus payments for themselves.[5,6]

For over 30 years, the World Health Organization (WHO) has advocated an essential medicines list for member states.[7] Every two years since 1977, WHO has updated the Model List of Essential Medicines with about 300 products, which countries are expected to adapt to their needs.[8] China's Ministry of Health developed its first National Essential Medicine List (NEML) in 1981, aiming to ensure the adequate supply, distribution, and appropriate use of essential medicines. The 2004 NEML consisted of 1,260 Chinese herbal preparations and 773 chemical and biological medicines products. However, appropriate supporting policies and mechanisms needed for the NEML to achieve its intended objectives have been lacking in the areas of manufacturing, supply, reimbursement and use of essential medicines.[3]

To guide the pharmaceutical sector, Chinese authorities have formulated a series of policies on pharmaceutical research and development, product approval, production, distribution, utilization, pricing, and insurance coverage.[9] Of these, price management and insurance coverage have been the two most important measures influencing the availability and use of essential medicines. Controls on medicines price have been promulgated 27 times since 1997, but the measures have not had significant impact in reducing the financial burden of service users. One reason is that manufacturers stop producing medicines that no longer had yield targeted profits, and hospitals and doctors are not keen to use them for similar reasons.[9-11]

Few studies have examined the availability and use of essential medicines in China, one of the four key health sector components targeted in China's ambitious 2009 health system reform

plan. In this paper, we provide evidence to answer the following research questions: 1) To what extents are essential medicines produced by Chinese manufacturers; 2) How available are these medicines in retail and hospital pharmacies? 3) How frequently and appropriately are essential medicines prescribed in Chinese health facilities?

METHODS

We conducted the study in Shandong and Gansu provinces, which are representative of the eastern (more developed) and western (less developed) regions of China respectively. To understand the availability of essential medicines, we conducted surveys in manufacturers, hospitals, and retail pharmacies in 2007. To understand medicines use patterns, we reviewed selected prescriptions collected from the studied hospitals. Table 1 contains an overview of the information collected from each data source. The study was funded by the World Health Organization, which agreed to the use of these data for academic research.

Table 1 Data sources for manufacturer, pharmacy, and prescription surveys

Provinces (population, n)	**Shandong (92 million)**			**Gansu (17 million)**		
Manufacturers, n	217			36		
Hospital level of care	Primary	Secondary	Tertiary	Primary	Secondary	Tertiary
Study hospitals, n	15	17	8	7	11	5
Prescriptions surveyed, n	982	1687	800	414	1078	495
Prefecture GDP/capita	High	Middle	Low	High	Middle	Low
City-level retail pharmacies, n						
With insurance contracts	2	2	2	2	2	2
Without insurance contracts	3	3	3	3	3	3
County level retail pharmacies, n	5	5	5	5	5	4

Manufacturer survey

All manufacturers in Shandong and Gansu provinces registered with the SFDA were requested to report to SFDA the essential medicines which were licensed by them for production and those which they actually produced in 2004 and 2005. We did not obtain data on non-essential medicines. In the structured interviews, we also asked the chief executives of these manufacturers which factors most influenced their production decisions.

Health facility pharmacy survey

We selected representative non-random samples of 10% of the primary, secondary, and tertiary care hospitals in each province. Hospital levels differ by technical capacity. Primary hospitals (known as urban community health centers and rural township health centers) deliver comprehensive primary care and limited inpatient care for common diseases. Secondary hospitals (known as urban district hospitals and rural county hospitals) are responsible for basic medical care, emergency care, and technical instruction to primary hospitals. Tertiary hospitals provide diagnosis and treatment for complex diseases and technical instructions to secondary hospitals.

In each health facility, we reviewed pharmacy procurement records to calculate the percentage of essential medicines to all western medicines purchased. We also assessed the availability of selected essential medicines in pharmacy stocks. Using structured questionnaires, we interviewed pharmacy managers about the reasons for procurement and stock of essential medicines.

Retail pharmacy survey

Hospital pharmacies dispense medicines for both outpatient and inpatient services. Retail pharmacies are managed by licensed pharmacists, can also dispense over the counter (OTC) and prescription medicines. We divided all prefectural level cities in the two studied provinces into three groups with high, middle, and low average GDP per capita. We randomly selected one studied city to represent each socioeconomic group; in each selected city, we purposively selected two insurance contracted retail pharmacies and three retail pharmacies without insurance contracts. We then purposively selected one middle GDP county (the administrative level below the prefectural level) in each studied city; in each selected county, we selected five representative retail pharmacies. In total, we surveyed 59 retail pharmacies, 30 in Shandong and 29 in Gansu province.

In the studied pharmacies, we assessed the availability of the studied essential medicines. The research team visited each pharmacy to collect the above data and to interview pharmacy managers about their rationale for procurement and stock of essential medicines and their understanding of the essential medicines concept.

Selection of survey medicines

To assess the availability of essential medicines in retail and hospital pharmacies, we randomly selected 40 traditional Chinese medicines (107 unique dosage forms) and 77 western medicines (98 unique dosage forms) from 1,260 traditional Chinese medicines and 773 western medicines listed on the 2004 NEML. Since product strength is not indicated on the NEML, we included any available strength of the studied western medicines. Although the availability of Chinese herbal preparations improves access to medicines especially in rural primary care, western medicines are the treatment of choice for the majority of Chinese patients.

Prescription review

Using clinic records, we reviewed outpatient prescriptions in each studied hospital on a random day in 2006, following the survey methods recommended by the World Health Organization for investigating prescriptions in health facilities.[12] This survey sought to characterize the proportion of prescriptions with essential medicines in routine adult outpatient care, as well as the rates of specific potentially inappropriate prescribing practices, including poly-pharmacy and over prescribing of antibiotics and injectables. We systematically selected 100 prescriptions in each

health facility. If fewer than 100 prescriptions were issued, we included all prescriptions issued on the study day. To assess the prescribing of western medicines, we excluded herbal products. To examine the potential over prescribing of antibiotics and injectables, we excluded prescriptions for children, adult emergency care, and adult cases treated in hospital infectious disease clinics.

Data analysis

Data were analyzed by using SPSS version 13.0. We summarized data on production as the percentage of licensed essential medicines manufactured, and identified the top 10 most frequently manufactured essential medicines. We summarized the supply of essential medicines in pharmacies by category (traditional Chinese medicines on the NEML, western medicines on the NEML, and medicines on the WHO EML). We listed the factors most frequently cited by the manufacturer chief executives and pharmacy managers for the decision of production of essential medicines. We also described the frequency of inappropriate prescribing using standard medicines use indicators.[13]

RESULTS

Manufacturing of essential medicines

Shandong manufacturers averaged 20 essential medicine product licenses in 2005, with about 60% of licensed products actually produced (Table 2). In Gansu, manufacturers averaged 41 licenses but only 50% of the products were manufactured in 2005. The proportion of essential medicines produced was not associated with manufacturer sales volumes. Among manufacturers that failed to report sale volumes, the proportion of licensed products actually produced was very low (1.1%).

Table 2 Essential medicines production as percentage of licenses held by manufacturers in Shandong and Gansu provinces in 2005, by manufacturer sales volume

Annual sales volume, CNY*	Shandong			Gansu		
	Manufacturers, n	Essential medicines licenses held, n	Licensed essential medicines produced, n (%)	Manufacturers, n	Essential medicines licenses held, n	Licensed essential medicines produced, n (%)
<10 million	54	440	271 (62)	13	262	102 (39)
10-30 million	51	778	463 (60)	12	610	306 (50)
30-100 million	48	1117	665 (60)	5	455	273 (60)
100-500 million	35	1292	872 (67)	3	136	57 (42)
>500 million	12	622	399 (64)	0	0	0
Unknown	17	91	1 (1)	3	26	0
Total	217	4340	2671 (62)	36	1489	737 (50)

Note: *On Jan 1, 2007, near the time of the survey, the conversion rate was CNY 7.80 to US $ 1.00.

In Shandong and Gansu provinces, the five factors mentioned by manufacturers as the most influential on the production decisions were market demand (81%, 94%), production cost (79%, 89%), price (65%, 50%), market share (54%, 56%), and profit margin (54%, 53%). Whether or not the medicines were listed by the social health insurance programs (32%, 25%) or listed in the NEML (20%, 25%) were less important.

At least one manufacturer produced 579 (28.5%) and 230 (11.3%) of the essential medicines on the 2004 NEML in Shandong and Gansu provinces respectively. The most frequently produced product was glucose injection (produced by 117 manufacturers in Shandong and 18 in Gansu). In Shandong, among the top ten most frequently manufactured products, eight were western medicines and six were injectables. Paracetamol tablets, a widely used pain reliever for adults and children, was among the top ten most frequently licensed products (by 36 manufacturers),

Table 3 Top 10 essential medicines products manufactured in 2005

Shandong			Gansu		
Medicine (name, dosage form)	**Manufacturers with license, n**	**Manufacturers producing, n**	**Medicine (name, dosage form)**	**Manufacturers with license, n**	**Manufacturers producing, n**
Glucose injection	177	117	Glucose injection	20	18
Sodium chloride injection	96	64	Xiaoyao pills	22	17
Glucose and sodium chloride injection	88	59	Liu Wei Di Huang pills	20	17
Banlangen granule	31	25	Bao He pills	17	14
Vitamin C injection	57	23	Gui Fu Di Huang pills	17	13
Metronidazole tablet	36	22	Bu Zhong Yi Qi pills	21	12
Norfloxacin capsule	37	21	Guipi pills	16	12
Ribavirin injection	35	21	Cen Su pills	15	12
Liu Wei Di Huang pills	30	21	Fuzi Lizhong pills	17	11
Metronidazole injection	29	20	Huang Lian Shang Qing pills	16	11

but was not among the top ten most frequently manufactured ones (by ten manufacturers). Among the top ten most frequently manufactured products in Gansu, glucose injection was the only western medicine (Table 3).

Supply of essential medicines

Retail pharmacies

Of the 140 western essential medicines randomly selected from the 2004 NEML, 49 (35%) and 69 (49%) were not available in any investigated retail pharmacy in Shandong and Gansu. Among the 41 NEML listed products not found in either province, 21 were injections, including diagnostics like technetium and iodohippurate, as well as products like potassium phosphate which require administration in hospital settings. However, essential medicines like salbutamol and sodium valproate syrups, used to treat asthma and epilepsy in children, respectively, were also not available. About two-thirds of the pharmacies stocked only 17% and 12% of the selected essential western medicines in Shandong and Gansu, respectively.

Of 107 essential traditional Chinese medicines, 7 (7%) and 19 (18%) products were not for sale in Shandong and Gansu provinces, respectively, including five which were not available in either province. About two-thirds of the pharmacies stored 45% and 46% of Chinese products in Shandong and Gansu, respectively.

Pharmacy managers in Shandong and Gansu reported that the top four factors determining their procurement decisions were market demand (90%, 100% respectively), price (90%, 83%), profit margins (73%, 45%) and market share (53%, 45%). Whether or not medicines are reimbursable by the social health insurance (33%, 34%) or listed in the NEML (10%, 21%) were again less important. In addition, more than 40% of pharmacy managers in each province did not know the NEML and 60% did not consider it in procurement decisions.

Hospital pharmacies

Essential medicine products constituted 67% (standard deviation, SD 27%), 72% (SD 22%), and 80% (SD 10%) of the western medicine products purchased in 2006 by primary, secondary, and tertiary care hospital pharmacies in Shandong, respectively. Of the randomly selected essential medicines products, pharmacies in Shandong primary care hospitals supplied a median of 26% and tertiary care hospitals 69% of the western medicines on the NEML; in Gansu, these figures were lower at 19% and 38% respectively (Table 4). However, supply in Shandong varied widely. One hospital pharmacy had less than 20% of the studied Western essential medicines, while another had more than 80%. Regardless of hospital level, half of the pharmacies carried about 25% of the Chinese NEML products. In Gansu province, no hospital pharmacy stocked more than 60% of Western essential medicines. Six NEML

products were not available in any surveyed hospital pharmacy in both provinces (pipotiazine injection, capreomycin injection powder, ritonavir oral liquid, compound salvia miltiorrhiza pills, niuhuang shangqing capsule, and buzhong yiqi decoction).

The most frequent reason for not stock the selected essential medicines across hospital levels was lack of clinical use for the products (in Shandong 64%, 58%, and 52% and in Gansu 62%, 69%, and 70% of primary, secondary, and tertiary hospitals, respectively, followed by availability of clinical alternatives (Shandong: 31%, 32%, 41%; Gansu: 28%, 28%, 22%).

Table 4 Availability (median percentage, 25th, 75th percentiles) of selected essential medicines in the sample of hospital pharmacies

	Shandong		Gansu	
Level of Care	**NEML-Chinese**	**NEML-Western**	**NEML-Chinese**	**NEML-Western**
Primary care	25% (21%, 36%)	26% (23%, 30%)	33% (17%, 33%)	19% (16%, 20%)
Secondary care	23% (20%, 33%)	47% (45%, 51%)	29% (22%, 34%)	30% (24%, 34%)
Tertiary care	23% (21%, 29%)	69% (61%, 74%)	23% (22%, 24%)	38% (37%, 43%)

Note: NEML means National Essential Medicines List.

Prescribing of essential medicines

Overall, as shown in Table 5, the average number of medicines prescribed per patient was lower in Shandong province and decreased by hospital level (an average of 3.2 medicines in primary, 2.5 in secondary, and 2.0 in tertiary level hospitals in Shandong, compared to 5.3, 3.9, and 2.6 in Gansu). However, despite prescribing fewer medicines, the costs per prescription (and thus cost per medicine) increased substantially by hospital level.

While the percentages of essential medicines prescribed ranged from 64% in tertiary facilities in Shandong to 86% in primary hospitals in Gansu, large proportions of prescriptions contained an antibiotic (between 34% in tertiary care hospitals in Shandong and 77% in primary care hospitals in Gansu) or an injection (from 22% in tertiary care to 61% in primary care hospitals in Gansu). The percentages of prescriptions containing an antibiotic or injection were higher at lower levels of hospital care in both provinces.

DISCUSSION

Our analyses showed that manufacturers in Shandong and Gansu provinces did not produce at least 40% of the products on the 2004 NEML for which they held production licenses, with their production decisions determined primarily by economic considerations. Many essential medicines are not perceived as profitable because of low demand, as well as price and mark-up controls.
Most retail pharmacies stocked less than 20% and most hospital pharmacies between 20% and

Table 5 Indicators (mean ±SD) of outpatient medicines prescribing for routine adult outpatient consultations*

	Shandong			Gansu		
Level of care (number of Rx)	**Primary (982)**	**Secondary (1687)**	**Tertiary (800)**	**Primary (414)**	**Secondary (1078)**	**Tertiary (495)**
Average number of medicines/Rx	3.2±0.7	2.5±0.4	2.0±0.3	5.3±2.0	3.9±1.1	2.6±0.5
Average cost/Rx(CNY) **	38.6±19.3	78.7±27.5	101.3±34.1	34.4±28.3	48.2±23.8	76.3±16.0
% Rx with EM	72.5±30.3	73.3±19.3	63.8±15.5	85.6±25.3	78.1±15.0	70.0±13.1
% Rx with reimbursable medicines	76.4±33.2	78.0±17.0	79.3±6.4	83.7±26.3	77.4±14.7	80.2±12.7
% Rx with antibiotics	53.9±9.1	45.9±11.9	33.6±14.0	77.2±18.5	59.6±8.7	40.7±6.0
% Rx with injections	41.7±11.2	31.8±16.3	27.4±16.3	61.1±28.5	36.6±14.0	22.3±9.4

Notes:

1. Rx=prescription;
2. * Pediatric, adult emergency care, and infectious disease clinic consultations were excluded;
3. ** On Jan 1, 2007, near the time of the survey, the conversion rate was CNY 7.80 to USD 1.00.

74% of randomly selected Western products on the NEML, depending on the province and hospital level of care. While retail pharmacies cited primarily economic reasons for their purchase decisions, hospital pharmacies most commonly cite lack of clinical utilization as the reason for not stocking medicines on the NEML. However, clinical and economic motivations are closely related. Pharmacies tend to stock what is prescribed, and prescribing is motivated in part by financial incentives. Clinicians in hospitals favor prescribing of higher cost medicines not subject to price controls because they generate greater revenues. This puts added cost burden on patients, especially for those without insurance who pay for all medicines out-of-pocket and also on both urban and rural health insurance funds.

A fairly high percentage of the medicines prescribed in adult hospital outpatient encounters were included on the 2004 NEML, which is not surprising given that the list contained 773 western essential medicines compared to the 300 on the World Health Organization Model Essential Medicines List. Antibiotics and injectables were very commonly prescribed. World Health Organization estimates that guideline-based care would result in rates of antibiotic use in routine outpatient care of 20% or less and rates of injection use of 5% or less.[12] A recent WHO global review reported that the median rates of outpatient antibiotic and injection prescribing were 46% and 19%, respectively, for all published studies conducted between 2004 and 2006.[14] These compare with the observed rates of antibiotic prescribing of 45% in Shandong and 59% in Gansu, and rates of injection prescribing of 34% and 38% in the two provinces, respectively. Thus, overprescribing of antibiotics and injectables in these two provinces is particularly inappropriate, in light of global standards.

Our study has several limitations. We did not collect data on non-essential products manufactured and thus we cannot assess the proportion of essential medicines manufactured among all medicines produced. We assessed the supply of the studied NEML medicines, rather than all NEML products. Although we randomly selected NEML medicines, it is possible that the studied medicines are not representative of all essential medicines. In addition, since the NEML does not specify whether medicines are appropriate for inpatient or outpatient care, some of the NEML medicines may not be expected to be stocked in retail pharmacies. Lastly, because we did not have diagnostic information related to individual prescriptions, we could not assess appropriateness of prescribing in relationship to the condition treated.

These limitations are not withstanding, the present data illustrate key challenges faced by the Chinese health care system. First, there are competing interests between the pharmaceutical industry's profit orientation and the government's objective of securing access to affordable essential medicines for the public. Over the past three decades, provincial and municipal governments have promoted the pharmaceutical industry as a pillar for economic growth and job creation,9,[15] without emphasizing its responsibility in helping to secure access to essential medicines.

Second, the current medicines pricing system has failed to stimulate competition in the production of essential medicines. The pricing authority strictly controls the price of generics, while allowing higher prices for branded generics and much higher prices for originator products. To avoid price controls, manufacturers have shifted registration and marketing to branded generics. The data from Shandong province, where the pharmaceutical industry is an important component of the economy[16] show that manufacturers give priority to Western injectables, among the more expensive products on the NEML.

Third, hospitals and doctors have no incentives to use relatively inexpensive generic essential medicines.[9,11] Since Government funding only accounts for about 10% of hospital funding,[17] hospitals and health care providers have relied on out-of-pocket payments by individual patients or health insurance reimbursement. Health facilities generate greater profits through prescribing of medicines with high mark-ups not subject to price control. The more medicines doctors prescribe, the higher the income hospitals and doctors receive.[5] Such perverse incentives have been a major obstacle in promoting appropriate use of medicines.

Consistent with other studies,[18,19] we find that essential medicines constitute a reasonably high proportion of the medicines prescribed in hospitals. However, some prescribing of essential medicines can be inappropriate, such as prescribing injectables for common conditions which can be safely treated with oral medicines or antibiotics for non-bacterial conditions in which they

are not indicated. In addition to the economic incentives to overprescribe expensive medicines, a lack of knowledge among patients about essential medicines and the absence of effective training on appropriate use of medicines for health care professionals likely contribute to high levels of inappropriate use.

The Chinese Government has embarked upon major changes to overcome these challenges.[20] In August 2009, the Ministry of Health issued a new National Essential Medicines List for primary health care institutions, consisting of 205 western generic medicines and 102 traditional Chinese products).[21] By 2012, all primary health care institutions with government subsidies in urban and rural areas will be required to stock and dispense these essential medicines with "zero mark-up". A maximum retail price will be set by the National Development and Reform Commission for each essential medicine and medicines with the same ingredient will have the same price, no matter whether the product is the originator, a branded generic, or a non-branded generic. All essential medicines will be covered by both urban and rural insurance schemes, and these medicines will be reimbursed at higher rates. Given the problems in the supply and use of the much larger 2004 NEML observed in this study, it will be important for the Government, insurance schemes, and health care institutions to establish policies and incentives that facilitate the use of the new NEML in manufacturing, procurement, and prescribing decisions at each level of the health care system.

CONCLUSION

In conclusion, we found that manufacturers, retail pharmacies, and hospital pharmacies paid limited attention to China's 2004 NEML in their decisions to manufacture, purchase, and stock essential medicines. We also found that prescribing of essential medicines was frequently inappropriate. These results should inform strategies to improve affordable access to essential medicines under the current health system reform.

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Chapter 3

The Effects of Clinical Interventions on Use of Medicines with a Focus on Antibiotics

3.1 Systematic Review of Interventions on Antibiotic Prophylaxis for Surgeries in Chinese Hospitals 2000–2012

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ABSTRACT

To systematically review intervention studies on antibiotic prophylaxis in clean or clean-contaminated surgery in Chinese hospitals from 2000 to 2012. Published peer reviewed articles, unpublished documents and reports, and gray literatures were identified through searching CNKI, CBM, VIP, PubMed (MEDLINE), WHO database, and the official websites of the Ministry of Health of China, provincial health authorities and medical university internal publications. Eighty-two studies were identified. Circulation and localization of central rules, regulations and guidelines; clinical pharmacists' involvement; technical, administrative, and managerial strategies were the mostly adopted interventions. Except one study, all claimed effectiveness of interventions. Limited effects were observed for non-indicated clean surgery. Huge gaps still existed between the international agreed guidelines and the claimed best performance following interventions. The following were critical to have more effective interventions: recognition, acceptance, and enforcement strategies of rules, regulations, and guidelines; intervention persistence and intensity; health information system; removal of health system perverse incentives; patient–doctor relationship; public education; and access to unbiased medicines information. A total 4 of 82 studies were pre–post studies with control; all others were simple pre–post studies without control. Simple measurement of the outcome indicators as an average for pre–post intervention groups and changes in between failed to distinguish the real intervention effect from confounding factors, and failed to adjust underlying trends. Interventions on surgical antibiotic prophylaxis in Chinese hospitals during 2000–2012 brought limited positive effects. There are still huge gaps between the Chinese situation and internationally agreed standards. More advanced study methodologies are needed to have better documentation of evidence of the most effective interventions.

BACKGROUND

World Health Assembly (WHA) resolutions urged member states to formulate measures to promote appropriate and cost-effective use of antibiotics.[1] The National Health and Family Planning Commission of P.R. China (formerly named the Ministry of Health, MoH) committed to this. They developed series regulations and rules on medicines use in health facilities. These included regulations on health facility pharmacy,[2] retail pharmacies sell antimicrobials with prescriptions,[3] national standard clinical guidelines for antibiotics use,[4] national antimicrobials clinical use and resistance monitoring network in hospitals,[5] standardized format of prescription and procedure of dispensing,[6] and restriction of antimicrobials stocked and used in different levels of public health facilities in 2012.[7]

Meanwhile, the World Health Organization (WHO) and the Chinese government jointly conducted interventions on antibiotics use in hospitals across China. Antibiotic prophylaxis in surgery was prioritized due to its severe inappropriate use in Chinese hospitals.[8] Beijing, Zhuhai, Guangdong, Jiangxi, Anhui, and Guangxi[9-14] reported the above interventions accordingly. Some local authorities followed this and conducted similar interventions to improve antibiotic prophylaxis in surgery.

MATERIALS AND METHODS

This study systematically identified and studied published peer reviewed articles, unpublished documents and reports, and gray literatures about antibiotic prophylaxis in clean or clean-contaminated surgery in Chinese hospitals during 2000–2012, and analyzed the effects of reported interventions and study methods, and the key determinants of antibiotic prophylaxis in surgery in Chinese hospitals.

Published peer reviewed articles were identified through searching CNKI, CBM, and VIP. Four Chinese terms were used to search the title, abstract and key words: prevention, antibiotics, antimicrobials, and intervention. Considering the possible difference between Chinese and English meaning of the same word, and only targeting studies about China, three English terms were used in searching the title and abstract of PubMed (MEDLINE): antibiotic prophylaxis, intervention, China. The study also reviewed reference lists of published articles to obtain earlier relevant articles.

In addition to peer reviewed literature, this study performed a systematic review of published and unpublished reports and documents. Chinese materials were obtained from the MoH and its working arms, such as the national antibiotics clinical use monitoring network, and other relevant research organizations. We searched the official website of MoH, provincial health authorities and medical university internal publications (including master and PhD thesis). English materials were obtained from WHO database of studies on use of medicines in developing and transitional countries. This database includes systematically

extracted information from published and unpublished articles and reports. It also contains information on interventions on medicines use reported by these studies. All studies in this database were published during 1990–2009. It has not been updated since 2009. Several relevant project reports of WHO country cooperation projects in China were identified through this way.

RESULTS

As showed in Table 1, 82 published studies were identified, which included eight articles of gray literatures (five in Chinese, three in both English and Chinese), and 74 peer reviewed articles (72 in Chinese, two in English). These articles contained studies about interventions on antibiotic prophylaxis in clean or clean-contaminated surgery in Chinese hospitals during 2000–2012. According to the infection control categories defined by the MoH,[15] 58 targeted category I incision (clean surgery), and 24 targeted category I and II incision (clean-contaminated surgery). A total 3 of 82 reviewed studies were published before 2005. The earliest published articles came from Beijing[9,10] and Guangdong[11,12,16,17] supported by WHO. A total 59 of 82 articles were published during 2010–2012, and came from provinces which participated in a WHO supported project.[10-12,14]

Table 1 Characteristics of 82 included articles

Category		***n***
Language		
	Grey literature	8
	Chinese	5
	Both English and Chinese	3
	Peer review articles	74
	Chinese	72
	English	2
Timing		
	2000-2004	3
	2005-2009	20
	2010-2012	59
Targeted surgery		
	Clean surgery	58
	Clean-contaminated surgery	24

All interventions were in public hospitals. As showed in Table 2, 81 of 82 reviewed articles were research articles,[9-14,16-21] and one was review paper containing evidence from other articles and reports.[18]

A total 4 of 81 research articles were pre–post studies with control.[13,14,19,20] A total 77 of 81 articles were simple pre–post studies without control. Although they named pre-group (non-intervention) as control group, they only measured the outcome indicators as an average for pre-group (non-

Table 2 Study method

Category	*n*
Research articles	81
Review articles	1
Pre-post with control	4
Pre-post without control	77
Similarity of cases considered between pre-post groups	10

intervention) before interventions, and for post-group (intervention) after interventions, and calculated changes in between.

A total 10 of 77 simple pre–post studies assessed the difference between pre-group (non-intervention group) and post-group (intervention group) in terms of age, sex, and severity of diseases,[16,21-25] or designed appropriate data collection plan to avoid seasonal variations.[16,21,22,26-29]

As shown in Table 3, a total 18 of 81 studies adopted rule, regulation and guideline approach. Circulation and localization of centrally developed rules, regulations and guidelines were common approaches; others were guideline training course and examination, newsletter and broader circulation, and experience sharing with other hospitals.[9-14,16,17,22-31]

A total 41 of 81 studies used clinical pharmacist to conduct interventions. Clinical pharmacist worked on-site with surgeons to decide antibiotics selection, dosage and strength, administration route and time, and took joint ward rounds. They collected drug utilization data, evaluated the degree of guideline compliance, gave feedback and recommendations to surgeons regularly.[9-14,19-29,31–54] 15 of 39 studies reported that clinical pharmacists conducted continued quality improvement initiative, for example, monitor-training-planning (MTP).[11–14,20,22,23,32,34,35,37,44,45,55,56] A total 13 of 39 studies claimed positive role of clinical pharmacist in improving antibiotic prophylaxis in surgery.26,[41–50,54,56]

A total 12 of 81 studies introduced electronic prescription and medical record management system. Electronic prescription and medical record management system were developed to achieve real time monitoring and evaluation of antibiotics use, and electronic control of antibiotics use (alert to non-compliance prescriptions).[16,19–22,25,27,42,43,53,57,58]

A total 12 of 81 studies adopted administrative and managerial strategy. Restriction of antibiotics prescribing rights of surgeons based on levels of technical skills; strengthening the accountability of hospital managers and department directors through signing commitment documents; setting up antibiotics clinical use supervision group under the leadership of hospital managers; integrating antibiotics use performance assessment into quality of care accreditation process; naming, shaming and economic punishment to bad performances, praising and rewarding to good performances.[19,23,26,29,57,59–65]

Table 3 Intervention approach

Intervention approach	*n*
Rules, regulations and guidelines approach	18
Clinical pharmacist	41
Electronic prescription and medical record management system	12
Administrative and managerial strategy	12

As shown in Table 4, all studies selected the following measurements based on Chinese national guidelines: antibiotics selection and changing, dose, solvent, admission routes and timing, and combination. A total 17 of 81 measured surgical site infection rate.[10,14,16,17,20–22,34,35,40,53,58,66–70]
A total 5 of 81 studies assessed adverse drug reaction rate.[19,29,41,49,71] A total 34 of 81 studies counted medical and medicines expenditures.[9,10,16,17,19–23,25,29,32,36,41,43,48,49,51,52,54,56,58,59,66–69,72–78] A total 9 of 81 studies compared duration of hospitalization.[20,29,30,41,44,66,67,74,79]

Table 4 Outcome measurement

Outcome measurement	*n*
Antibiotics selection and changing, dose, solvent, admission routes and timing, combination	81
Surgical site infection rate	17
Adverse drug reaction rate	5
Medical and medicines expenditures	34
Duration of hospitalization	9

As showed in Table 5, only one study claimed failure in improving antibiotic prophylactic in a Chinese hospital,[80] all others concluded effectiveness of interventions. There were limited effects on non-indicated clean surgery, especially clean-contaminated surgery. This was because that surgeon concerned about failure to control hygiene risks in operating theatres, and patients' complains in case of having infections.[12,17,40,44,81–83]

A total 24 of 81 studies reported that the proportion of clean surgery used antibiotics reduced from 21.3–100% to 3.2–90%;[18,23,25,35,37,41,44–46,56,58,59,66,74–76,79,80,84–89] 9 of 81reported that the proportion of antibiotic prophylaxis 0.5–2 hours before incision increased from 7.7–60% to 31–92%; [20,25,37,45,47,60,72,77,88] 5 of 81 reported that the proportion of antibiotic prophylaxis <24 hours increased from 0–5% to 46–81%;[23,45,47,76,90] 2 of 81 reported that the proportion of cases used no antibiotics after operation increased from 0–62% to 39–96%;[36,91] 26 of 81 reported that the No. of days for antibiotic prophylaxis reduced from 2–16 to <24 hours-11;[11,12,18,29,34,36–38,42–49,52,56–58,60,65,69,70,78,81] 9 of 81 reported that the proportion of combination therapy reduced from 4–100% to 0–21%;[11,12,29,41,48,55,58,67,75] 7 of 81 reported that the number of days for hospitalization reduced from 6–16 to 2–6.[28,29,32,44,66,70,74]

Table 6 Quantitative intervention effect of three controlled studies

Included study	Indicator	Intervention group		Control group	
		Pre-intervention	Post-intervention	Pre-intervention	Post-intervention
WHO Project[13] & Zheng[14]	Rationality scores of indicated clean surgery with antibiotic prophylaxis	55.4[a]	77[b]	57.6[a]	64.3[b]
	Proportion of non-indicated clean surgery admitted no antibiotics	61.9%[c]	60.9%[d]	84.4%[c]	59.1%[d]
Sun[20]	Proportion of non-indicated clean surgery with antibiotic prophylaxis	75%[e]	32.56%[e]	44.23%[f]	42.05%[f]
	Proportion of clean surgery admitted no antibiotics after operation	0.96%	39.5%	0	1.1%

Notes:

a. t-test P> 0.05, no significant difference between intervention and control group pre intervention.

b. t-test P< 0.05, significant difference between intervention and control group post intervention.

c. Chi2-test P< 0.05, significant difference between intervention and control group pre intervention.

d. Chi2-test P> 0.05, no significant difference between intervention and control group post intervention.

e. P < 0.05, significant difference of intervention group pre and post intervention.

f. P > 0.05, no significant difference of control group pre and post intervention.

Table 5 Outcome of intervention

Measurement	Outcome	No. of research articles
Overall effect of intervention	Effective	80/81
% of clean surgery used antibiotics	Reduced from 21%-100% to 3%-90%	24/81
% of antibiotic prophylaxis 0.5-2h before incision	Increased from 7.7%-60% to 31%-92%	9/81
% of antibiotic prophylaxis <24 h	Increased from 0-5% to 46%-81%	5/81
% of cases used no antibiotics after operation	Increased from 0-62% to 39%-96%	2/81
No. of days for antibiotic prophylaxis	Reduced from 2-16 to <24 h-11	26/81
% of combination therapy	Reduced from 4%-100% to 0-21%	9/81
No. of days for hospitalization	Reduced from 6-16 to 2-6	7/81

The outcome reported by the three controlled studies was summarized as showed in Table 6. The WHO supported project[13] and Zheng[14] found that, the rationality scores of indicated clean surgery with antibiotic prophylaxis of the intervention group increased from 55.4 to 77.0, and that of the control group also increased from 57.6 to 64.3.

The difference between the intervention and control group was not significant before interventions (p>0.05), but was significant following interventions (p<0.05). This implied positive effect of interventions on increasing the rationality scores of indicated clean surgery with antibiotic prophylaxis.

The proportion of non-indicated clean surgery with antibiotic prophylaxis of the intervention group slightly dropped from 61.9% to 60.9%, while that of the control group significantly dropped from 84.4% to 59.1%. The difference between the intervention and control groups was significant before intervention (p<0.05), but was not significant (p>0.05) following interventions. This indicated other factors to affect surgeons' decision on antibiotics use for non-indicated clean surgery, such as health system problems and patients' expectations. Sun[20] considered similarity

Table 7 Surgical prophylaxis guidelines & reported best performance after intervention in Chinese hospitals

Key indicators	World Alliance for Patient Safety (2nd edition)[92]	Scottish NHS Guideline July 2008[93]	Chinese National Guideline 2008[4]	Reported best performance after intervention in Chinese hospitals
General principle	NA	Grades of recommendations based on levels of evidence	Not recommended in general, except high risk factors	32.6%-39.1% non-indicated clean surgery with antibiotic prophylaxis[14,20]
Timing	Within the hour before incision	Intravenously ≤30 minutes before the skin is incised	0.5-2 hours before surgery	31.4%-92.4% antibiotic prophylaxis 0.5-2 hours before surgery[23,36,45,73]
Dosage and duration	NA	Single standard dose is sufficient under most circumstances. Additional dosage may be indicated for longer surgery or shorter-acting agents, and intra-operative blood loss in adults (>1,500 ml)/children (25 ml/kg) after fluid replacement. Duration<24 hours	Single dose for clean surgery <2 hours. 2nd dose could be given when surgery >3 hours or blood loss >1,500 ml. Duration<24 hours, could be prolonged to 48 hours for specific circumstances	39.5%-96% of clean surgery with no antibiotic prophylaxis after operation,[20,34] average number of days for antibiotic prophylaxis was 4.1±2.9 (X ± SD)[13,14]
Medicines choice	NA	Narrow spectrum, less expensive antibiotics should be the first choice.	Effectiveness, safety, convenience, and cost should be considered	2nd & 3rd generations of cephalosporins were the most commonly used antibiotics[22,34,47,67,79]

of the studied cases in the control and intervention groups. Proportion of clean surgery with antibiotic prophylaxis of the intervention group significantly decreased from 100% to 60.5% ($p<0.05$), while that of the control group changed from 100% to 98.9% ($p>0.05$). Proportion of clean surgery without antibiotic prophylaxis after operation of the intervention group significantly increased from 1.0% to 39.5% ($p<0.05$), while that of the control group changed from 0 to 1.1% ($p>0.05$). Proportion of non-indicated clean surgery with antibiotic prophylaxis of the intervention group significantly reduced from 75.0% to 32.6% ($p<0.05$), while that of the control group changed from 44.2% to 42.1% (not significant, $p> 0.05$).

The best performances claimed by the reviewed studies were compared with the international guideline, the internationally recognized national guideline, and the Chinese national guideline in Table 7. Although Chinese national guideline recommends that antibiotic prophylaxis is not necessary for non-indicated clean surgery, 32.6–39.1% of them still used antibiotics; 31.4–92.4% cases were in line with the recommendation of international and national guidelines: antibiotic prophylaxis 0.5–2 hours before incision; 39.5–96.0% of clean surgery did not use antibiotics after operation, the average number of days using antibiotics was 4.1 ± 2.9 (X ± SD), although both the Scottish and Chinese national guideline recommend that single standard dose is sufficient under most circumstances, and duration for antibiotic prophylaxis should <24 hours for special cases; Narrow spectrum antibiotics were recommended by the Scottish Guideline, Class II and III generations of cephalosporin were the most commonly used antibiotics.

DISCUSSION

Intervention effect evaluation criteria

Even though the Chinese guideline is generally not as stringent as the international/internationally recognized national guidelines, huge gaps still existed between the Chinese guideline and the claimed best performances following interventions. This indicates that, the situations after intervention are still not optimistic.

Lessons learnt from the reviewed literature

According to the experiences summarized by the reviewed literature, the following aspects are critical to have more effective interventions:

Enforcement of rules and regulations and guidelines

The MoH of China issued a series of rules and regulations and guidelines. Most of them were general principles but not operational details. Putting them into good practice in hospitals was problematic without effective implementing strategies. Identification and recognition of centrally issued rules and regulations and guidelines based on actual situation, and developing operational implementation strategies were crucial for better enforcement.[13,14,18,27,48]

Acceptance and compliance of guidelines

Contradictions exist among guidelines issued by different government agencies and professional associations. Well organized expert consultation process and standardized evidence-based mechanism for guideline development are premise for more authoritative guideline and better acceptance and compliance at local levels.[14,18]

Intervention intensity

Promoting appropriate use of antibiotics requires continued efforts, one-time project based intervention, or pure executive order won't have sustainable effects.[11–14,18,25,35,38,59] Continued efforts with repeated MTP circles have better effects on changing prescribing behaviors than pure guideline circulation and training.[11–14,20,22,23,34,35,37,44,45,55,56] Naming and shaming, economic punishment for bad performances, praising and rewarding to good performances are helpful for better guideline compliance.[19,23,26,29,57,59–65]

Health information system

Electronic prescribing management system enables real time monitoring of antibiotics prescribing, timely alert of prescriptions not complied with guidelines, and easy utilization analysis. It is an efficient tool for easy regular monitoring, data collection, evaluation, feedback, and information sharing.[16,19–22,25,27,42,43,53,57,58]

Health system problems

Technical interventions have limited effect in convincing surgeons not to use antibiotics for non-indicated cases. Complicated problems exist which are beyond the knowledge and prescribing habits of surgeons. Perverse incentives in health systems have driven doctors to use expensive and broad spectrum antibiotics even for non-indicated cases.[18] These perverse incentives include prices of both labor and skill extensive medical services are set by the government far below the real cost, surgeons have to rely on selling medicines and diagnostic tests to collect revenue and to compensate low salary.

Patient–doctor relationship

Poor accessibility and affordability to quality care and low formal salary but heavy workload have brought huge pressures to both patients and doctors. Such pressures lead to deteriorated patient–doctor relationship. Placing the responsibility of proof on doctors in medical disputes about unexpected infections may also be a factor for inappropriate antibiotic prophylaxis. Surgeons are risk-averse for those clean contaminated surgeries, and high risk ones, such as cesarean section.[11,12,14,18,20,23,39,58,62]

Public education

Public education on prudent use of antibiotics is weak.[9,14,18,20,70] General public always have

incorrect perceptions about antibiotic use for cold, cough, fever, and other non-bacterial infections. People always regard the brand new and broad-spectrum antibiotics as "big guns."

Unbiased medicines information

Clinical pathway and guideline are just newly introduced and not yet accepted nationwide. Timely access to evidence-based medicines information has been weak in less developed areas. There is no well recognized, officially launched, friendly and public accessed channels for evidence-based medicines information dissemination.[14,18]

Intervention effect evaluation method

Making conclusions on successfulness of intervention needs rigorous research methods. There is a need for adopting more advanced method for policy impact analysis. Lots of studies claimed positive effects. However, simple pre–post study without control failed to distinguish the real intervention effect from the confounding factors. Simple before-after comparison without consideration of difference between pre-group (non-intervention) and post group (intervention) and seasonal variations, could not adjust underlying trends. In addition, calculating average outcome measurement for pre–post groups, and not using advanced statistical techniques (such as segmented regression) to analyze the data, was a rough estimation rather than an accurate quantification.

CONCLUSION

Interventions on antibiotic prophylaxis in clean and clean contaminated surgery in Chinese hospitals during 2000–2012 brought limited positive effects. There are gaps between the Chinese situation and international standards. It is not yet a time for concluding a successfulness of these interventions. Simple pre–post study without a well designed control group might not be appropriate for drawing any conclusions of the intervention effect. The most outstanding problem for interventions is non-indicated antibiotic prophylaxis. This indicates that there might be complex factors which affected surgeons' antibiotic prophylaxis decision making, such as health system problems and patients' expectations. More comprehensive approaches and continued efforts are needed. More advanced methodologies are needed to better document evidences for the most effective interventions, and to inform the policy makers more effectively.

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Chapter 3

The Effects of Clinical Interventions on Use of Medicines with a Focus on Antibiotics

3.2 Changes in patterns of antibiotic use in Chinese public hospitals (2005–2012) and a benchmark comparison with Sweden in 2012

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ABSTRACT

The changes in the patterns of antibiotic use in Chinese hospitals before and after intensive nationwide interventions are reported, and compared with Chinese national targets and antibiotic use in Swedish hospitals. Chinese data were collected quarterly and yearly from selected patient prescriptions/medical records and medicines inventory control systems from 15 hospitals (2005-2012). Swedish data were extracted from a 2010 point prevalence survey and 2009-2012 sales data from seven university hospitals. An interrupted time series with segmented regression analysis was used to measure changes in the patterns of antibiotic use in Chinese hospitals before and after the 2011 interventions. Following the 2011 interventions, significant reductions of antibiotic use in Chinese hospitals were seen: the proportion of prescriptions with antibiotics decreased 4.7% (p=0.03), and the proportion of medical records with antibiotic prescription decreased 7.3% (p=0.04). The proportions of prescriptions and medical records with antibiotic in Chinese hospitals in 2012 was 10% and 50%, respectively, and remained much higher than Swedish hospitals (1.1% in DDDs for outpatients and 34% in number of patients for inpatients). Inpatient consumption in Chinese hospitals significantly dropped from 910 DDD/1 000 inpatient days in 2008 to 473 in 2012 (588 in Swedish hospitals). Antibiotics are being used less frequently in Chinese hospitals, broad spectrum antibiotics are still preferred, and overall usage is higher than Sweden. A significant reduction of overall inpatient antibiotic consumption was observed the 2011 interventions. It is not possible to identify whether the changes have resulted in less inappropriate antibiotic use. Further studies are needed.

INTRODUCTION

Over-prescription of antimicrobials and increasing antimicrobial resistance are major public health issue in China as well as a significant challenge to global health. The World Health Assembly called member states to promote rational antibiotic use to contain antimicrobial resistance.[1] As a result, the Chinese government have issued and implemented a number of policies.

To assess the impact of these actions, a study was undertaken as part of the Plan of Action for Sino-Swedish Health Cooperation 2011-2014. The collaboration aims to apply Swedish expertise in promoting appropriate use of antibiotics and to motivate the ongoing work in China. Sweden has been used as a benchmark because of its well-established and effective policies and legislation on antibiotic use.[2] Sweden was also one of the first countries to initiate a cross-stakeholder cooperation for the containment of antibiotic resistance (Swedish strategic programme against antibiotic resistance, STRAMA).[3] These long-term and structured interventions have proved a success, as Sweden has a low use of antibiotics and resistance rates.[4-7]

The health systems of China and Sweden are very different, Sweden being a country with a small population (9.5 million) compared with China (1.3 billion). Swedish hospitals are largely publicly owned and the primary healthcare system is universal and effective. Most patients enter the health system via the primary care.[8-11] In contrast, the capacity of the primary healthcare providers is still under development in China, especially in the extensive rural areas that lack skilled staff and modern equipment. Healthcare delivery relies predominantly on hospital-based care, with public tertiary hospitals being the main healthcare providers. Primary care institutions do not play a dominant role in providing outpatient services, and most patients directly accessing hospitals even for common diseases, as evidenced by only 41% of outpatient visits being provided by primary care in 2012.[12,13]

This study measured the changes in patterns of antibiotic use and inpatient consumption in Chinese public general tertiary hospitals from 2005 to 2012, which covered the period before and after the 2011 interventions. The 2012 observations in Chinese hospitals were also compared with the Chinese national targets and Swedish hospitals.

Policy impact analysis in China usually uses simple before and after comparison. Rigorous research studies using more sophisticated methods that can make more precise measurement of policy impact are few.[14] To our knowledge, this is the first assessment of the effect of interventions has on antibiotic use using a longitudinal study with interrupted time series data and segmented regression analysis. This methodology is the strongest quasi-experimental design to evaluate longitudinal effects of time-delimited interventions.[15]

MATERIALS AND METHODS

Study design

Changes in the patterns of antibiotic use in Chinese hospitals before and after the 2011 interventions (during March 2005 to December 2012) were measured and the 2012 observations in Chinese hospitals were compared with the Chinese national targets[16,17] and with Swedish hospitals.

The 2011 interventions were the most intensive and far-reaching initiative of the Ministry of Health aimed to improve antibiotic use in hospitals. Following extensive advocacy and mobilization across the country, all levels of governments officially announced the interventions in written documents, and circulated the documents to each hospital. The internationally accepted concept of "antibiotic stewardship" was integrated into these measures. Many coordinated measures were taken,[16-18] including (a) setting targets; (b) strengthening accountability; (c) auditing clinical indications for antibiotic use; (d) building the capacity of infection control; (e) defining the prescribing of specific antimicrobials for different levels of professionals in clinical practice; (f) restricting the number of agents prescribed; (g) conducting regular antimicrobial resistance monitoring with an alert system for multi-resistance; (h) organizing guideline training; (i) conducting a monthly outpatient prescription and inpatient medical record audits, identifying the prescribers who are continuously not able to achieve the targets set by an individual hospital, and revoking prescribing rights for the frequent outliers; (j) setting up monitoring networks across hospitals and regions to share information at national and local levels; (k) carrying out unannounced inspections at the targeted public hospitals; and (l) sharing good practice. Specific targets were set by the Ministry of Health as follows: the proportions of outpatient (OP) prescriptions and inpatient (IP) medical records with the prescription of antibiotics to be <20% and <60%, respectively. All antibiotic prophylaxis should be given before incision (except for Cesarean section) and patients receiving antibiotic prophylaxis should not be >24 h (except certain specific conditions), and the total IP consumption of antibiotics for systemic use (J01) to be <400 DDD/1 000 inpatient days.

Outcome measures

Severn indicators to measure the pattern of antibiotic use in hospitals were defined: (a) the proportion of OP prescriptions given for at least one antibiotic (including oral and parenteral); or (b) one parenteral antibiotic prescribed; (c) the proportion of IP medical records with a prescription for at least one antibiotic; or (d) one parenteral antibiotic prescribed; (e) the proportion of patients receiving antibiotic prophylaxis before incision; (f) the proportion of patients given antibiotic prophylaxis for >24 hours; and (g) the total IP antibiotic consumption (DDD/1 000 inpatient days).

"Inpatient days" were calculated by multiplying the annual total number of hospital discharges (ranging between 15,425-193,000 in various study hospitals during 2005-2012) with the mean number

of days of hospitalization (discharge date minus admission date for admitted patients in each study hospital; for patients who were discharged on the same day of hospitalization, the number will be regarded as 1. IP antibiotic consumption was measured for antibiotics for systemic use (J01), and specific Anatomical Therapeutic Chemical (ATC) 3 and ATC 4 classes. These classes include penicillins (J01C), quinolones (J01M), 1st–4th generation cephalosporins (J01DB–DE), carbapenems (J01DH), and macrolides (J01FA), of which the Chinese antibiotic classification system and the ATC system are similar to each other.

Study population, setting, and data source

China

The 35 hospitals, all public general tertiary hospitals of the National Antimicrobial Clinical Use and Resistance Monitoring Network (which started to collect antibiotic clinical data in 2005), were categorized by geographic regions (six in total across the country). Two member hospitals from each region were chosen, which were located in a city with a mean income level for each region. In addition one was added to each of the three regions with the highest populations. The 15 targeted hospitals had 600-4 300 beds, 2 800-12 600 daily OP and emergency visits, and 91-375 daily discharges.

Longitudinal data for antibiotic use (indicators a-f) were extracted from selected prescriptions and medical records from the 15 study hospitals. In each hospital, 100 prescriptions, 15 surgical records and 15 non-surgical records were randomly selected from the OP adult prescriptions given on the 16th and patients discharged during 11th-20th of the first month of each quarter during 2005-2010 and of each month during 2011-2012. In each quarter during 2005-2010, a total of 1 500 prescriptions, 225 surgical records and 225 non-surgical records were randomly selected. In each quarter during 2011-2012, a total of 4 500 prescriptions, 675 surgical records and 675 non-surgical records were selected. Following the practice of the national monitoring network, the departments of emergency, pediatrics, infectious diseases, and care for senior government officials were excluded from the sampling of OP prescriptions. Antibiotic consumption pressures (indicator g) were collected annually from the medicines inventory control systems of the 15 studied hospitals (2005-2012).

Sweden

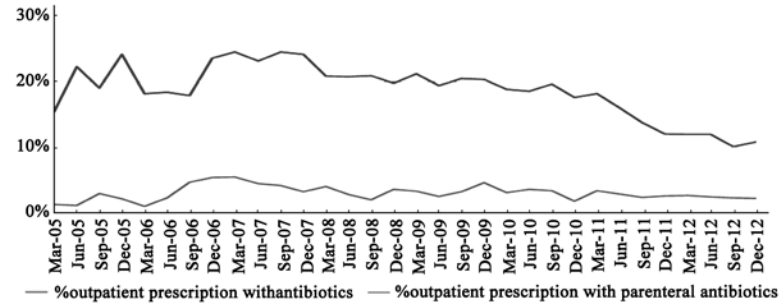
The 2009-2012 annual sales data were collected from all seven public tertiary hospitals in Sweden (university hospitals, 550–2 000 beds) to measure the IP antibiotic consumption. OP antibiotic and parenteral antibiotic use and IP antibiotic consumption data for indicators a, b, and g were extracted from 2012 sales data of the seven university hospitals. Data for IP antibiotics and parenteral antibiotic use, proportion of patients given antibiotic prophylaxis for >24 hours for indicators c, d, f were obtained from the most recent 2010 point prevalence survey.

Data analysis

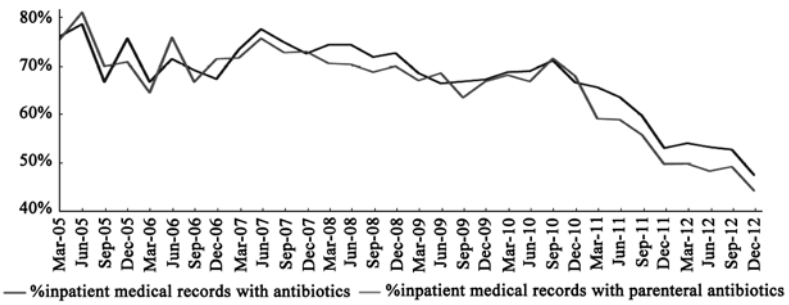
The quarterly antibiotic use data collected from the OP prescription and IP medical record data for the Chinese hospitals was plotted (March 2005 to December 2012) (Fig. 1). Annual antibiotic consumption for Chinese and Swedish hospitals during 2005–2012 for systemic use and for specific ATC categories as DDD/1 000 inpatient days and proportions consumed are shown in Fig. 2.

Fig. 1 Proportions of (A) outpatient prescriptions of antibiotic and (B) inpatient medical records with antibiotic, and (C) proportions of surgical patients given antibiotic prophylaxis before incision and for a duration of >24 h in Chinese hospitals. **Data source:** selected outpatient prescriptions and inpatient medical records from 15 Chinese public tertiary general hospitals.

(A)



(B)



(C)

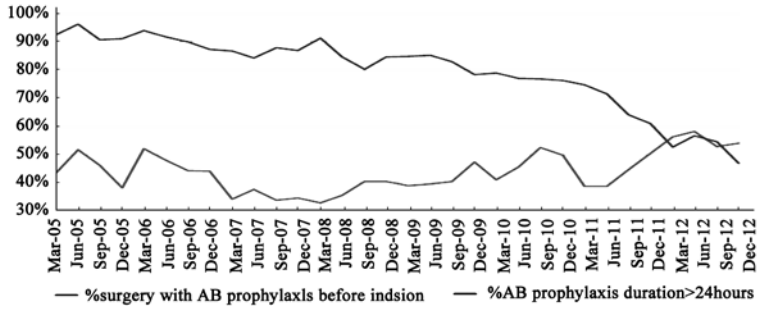
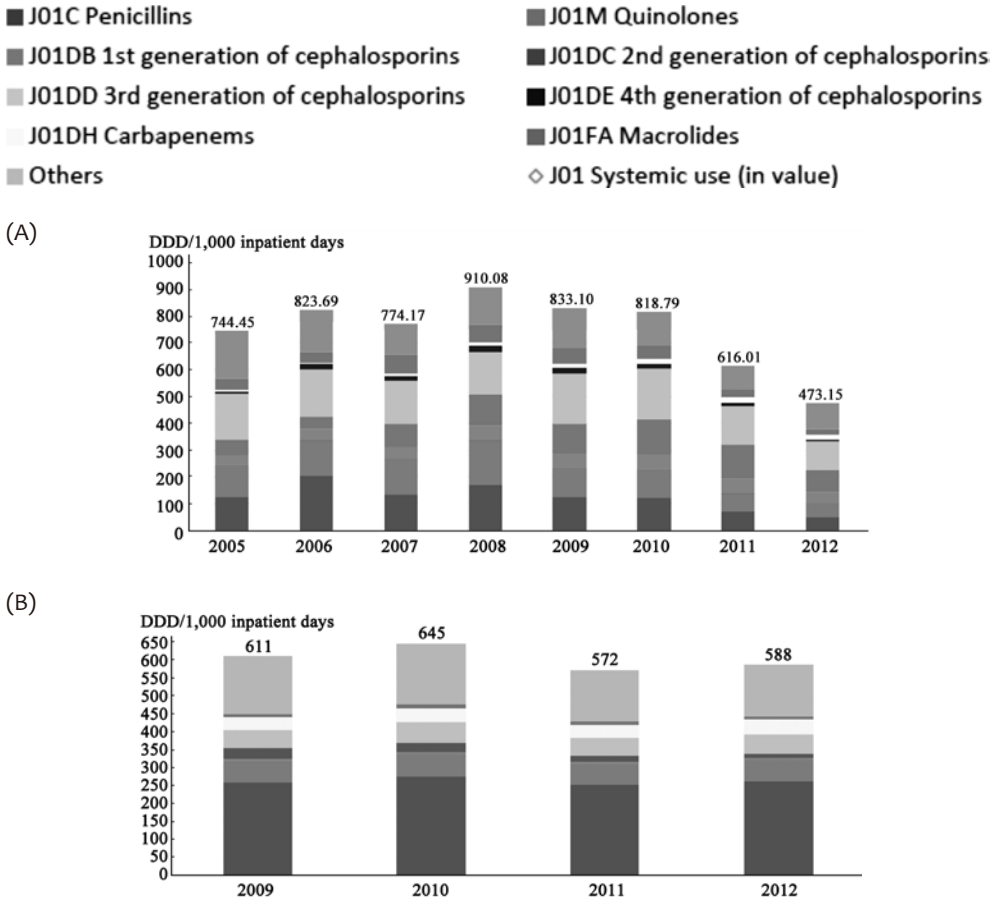


Fig. 2 Inpatient antibiotic (J01 systemic use) consumption by Anatomical Therapeutic Chemical (ATC) categories in (A) Chinese and (B) Swedish hospitals. Sources: (1) China: medicines inventory control systems of 15 Chinese public general tertiary hospitals; (2) Sweden: sales data of seven Swedish university hospitals. **Notes:** (1) The ATC classes not measured (J01A, J01B, J01DF, J01DI, J01 E, J01FF, J01FG, J01G, J01MB and J01X) are included as 'Others' in the bar; (2) Inpatient antibiotic consumption pressure is calculated as defined daily doses (DDD) per 1000 inpatient days.



Longitudinal time series quarterly data were analyzed using a segmented linear regression model to assess changes in levels and trends after the 2011 interventions in Chinese hospitals. Time series data analysis statistical software can control for auto correlated errors, which controls for secular trends and can also adjust for potential serial correlation of the data.[15,19] Although the announcement of the interventions was issued in April 2011, implementation started in August 2011. Considering that the study collected quarterly data from Chinese hospitals in 2011, September 2011 was adopted as the starting time point of the interventions for conducting segmented regression analysis. Changes in trends before and after September 2011 and the change in levels in September 2011 were compared using Stata 12.0 (StataCorp LP, College Station, TX).

Data for China and Sweden were compared Data for China and Sweden were compared using 2012 indicators (a–g) for Chinese hospitals, and the 2012 Swedish sales data and 2010 -point prevalence survey data. using 2012 indicators (a-g) for Chinese hospitals, and the 2012 Swedish sales data and 2010 point prevalence survey data.

RESULTS

Changes in antibiotic use in Chinese hospitals before and after the introduction of the 2011 interventions

The proportion of OP prescriptions with parenteral antibiotics was stable at < 6% (Fig. 1). With the exception of antibiotic prophylaxis, which increased from 40 to 50% (pre-2011) to 50-60% (post-2011), all other indicators steadily decreased, as did OP prescriptions (20% to 10%). The proportion of IP medical records with antibiotics and parenteral antibiotics both decreased from 60 to 80% to around 50%. The proportion of patients given antibiotic prophylaxis for >24 h decreased from 70 to 90% to 60%.

Data are also presented on the trends in IP consumption of some targeted antibiotic ATC classes (Fig. 2). Consumption of antibiotics for systemic use (J01) was highest in 2008, thereafter decreasing afterwards, particularly during 2011-2012, as did other classes.

Segmented regression analysis of the quarterly data (Table 1) showed that, before September 2011 ,OP and IP antibiotics use (indicators a and c), IP parenteral antibiotic use (indicator d), and patients given antibiotic prophylaxis for >24 hours (indicator f) had already decreased significantly, (p=0.004, p=0.002, p<0.001 and p<0.001, respectively) from the start of the study. OP parenteral antibiotic use (indicator b) steadily increased and antibiotic prophylaxis given before incision (indicator e) steadily decreased.

In September 2011, the proportion of OP prescriptions given for at least one antibiotic (indicator a) and the proportion of IP medical records with at least one antibiotic (indicators b) significantly dropped by 4.7% (p=0.03, 95% CI [−8.91%, −0.56%]) and 7.3%(p=0.04, 95% CI -14.2 to -0.4), respectively. The proportion of IP medical records with at least one parenteral antibiotic prescribed (indicator d) and the proportion of antibiotic prophylaxis duration>24 h (indicator f) both dropped significantly by 8.6% (p=0.03, 95% CI -16.1% to -1.1%; and p=0.003, 95% CI 13.9% to 3.3%), respectively. The proportion of OP prescriptions given with at least one parenteral antibiotic (indicator b) and the proportion of antibiotic prophylaxis given before incision (indicator e) steadily decreased.

After September 2011, antibiotic prophylaxis duration>24 h (indicator f) significantly decreased (p=0.002), the other indicators not changing significantly.

We also observed the trends of IP consumption pressures of the targeted antibiotic ATC classes, as

shown in Fig. 2. The consumption pressure of antibiotics for systemic use (J01) reached the highest level in 2008, shifted to decrease afterwards, and decreased faster during 2011-2012. Other classes had similar trend changesAfter September 2011, antibiotic prophylaxis of duration >24 h (indicator f) significantly decreased (P = 0.002), with the other indicators not changing significantly.

Segmented regression analysis of the quarterly data (Table 1) showed that, before September 2011 OP and IP antibiotics use (indicators a and c), IP parenteral antibiotics use (indicator d), and antibiotic prophylaxis duration>24 hours (indicator f) already decreased significantly, (p=0.004, p=0.002, p<0.000 and p<0.000). OP parenteral antibiotics use (indicator b) steadily increased, but antibiotic prophylaxis before incision (indicator e) steadily decreased.

In September 2011, the proportion of OP prescriptions given for at least one antibiotic (indicator a) and the proportion of IP medical records with at least one antibiotic (indicators b) significantly dropped 4.7% (p=0.03, 95% CI [−8.9%, −0.6%]) and 7.3% (p=0.04, 95% CI [−14.2%, −0.4], respectively). The proportion of IP medical records with at least one parenteral antibiotic prescribed (indicator d) and the proportion of antibiotic prophylaxis duration>24 hours (indicator f) both significantly dropped 8.6% (p=0.03, 95% CI [−16.1%, −1.1%]) and (p=0.003, 95% CI [−13.9%, −3.3%]), respectively. The proportion of OP prescriptions given for at least one parenteral antibiotic (indicator c) and the proportion of antibiotic prophylaxis before incision (indicator e) steadily decreased.

After September 2011, antibiotic prophylaxis duration>24 hours (indicator f) significantly decreased (p=0.002), with the other indicators did not changing significantly.

Comparison of antibiotic use in Chinese and Swedish hospitals

Table 2 shows that 10% of OP prescriptions and 50% of IP medical records include a prescription for antibiotics in Chinese hospitals. These are below the Chinese national targets (<20% and <60%) but higher than Swedish hospitals (1.1% and 34%). Use of parenteral antibiotics for OP prescriptions (2%) and IP (46%) in Chinese hospitals is much higher than Swedish hospitals (0.001% and 15%). The use of antibiotic prophylaxis is much poorer in China compared to Sweden, with only 55% of prophylaxis being given before incision and 56% of prophylaxis having a duration >24 h. Both values are above the Chinese national targets are much worse than Swedish hospitals (1.1% and 34%). IP antibiotic consumption for systemic use (J01) in Chinese hospitals was 473 DDD/1 000 inpatient days, which is higher than the Chinese national target (<400 DDD/1 000 inpatient days)[17] but lower than Swedish hospitals (588 DDD/1 000 inpatient days).

Table 1 Segmented regression analysis results comparing antibiotic use before, during, and after the 2011 nationwide interventions in China, 2005–2012

Independent Variables		Coefficient[a]		SE	P-value[b]	95% CI
(a)	% of OP prescriptions with antibiotics	Constant β0	22.8	0.8	0.000	21.2, 24.5
		Secular trend β1	**–0.2**	**0.05**	**0.004**	**–0.3, –0.06**
		Change in level β2	**–4.7**	**2.0**	**0.03**	**–8.9, –0.6**
		Change in trend β3	–0.4	0.5	0.4	–1.4, 0.6
(b)	% of OP prescriptions with parenteral antibiotics	Constant β0	**2.6**	**0.7**	**0.001**	**1.1, 4.1**
		Secular trend β1	0.04	0.05	0.4	–0.06, 0.1
		Change in level β2	–0.7	1.1	0.5	–3.0, 1.6
		Change in trend β3	–0.1	0.3	0.7	–0.8, 0.5
(c)	% of IP medical records with antibiotics	Constant β0	74.7	1.4	0.000	72.0, 77.5
		Secular trend β1	**–0.3**	**0.09**	**0.002**	**–0.5, –0.1**
		Change in level β2	**–7.3**	**3.4**	**0.04**	**–14.2, 0.4**
		Change in trend β3	–1.5	0.8	0.07	–3.2, 0.2
(d)	% of IP medical records with parenteral antibiotics	Constant β0	75.2	1.5	0.000	72.2, 78.2
		Secular trend β1	**–0.4**	**0.1**	**0.000**	**–0.6, –0.2**
		Change in level β2	**–8.6**	**3.7**	**0.03**	**–16.1,–1.1**
		Change in trend β3	–1.3	0.9	0.14	–3.1, 0.5
(e)	% of antibiotic prophylaxis before incision	Constant β0	**42.8**	**3.7**	**0.000**	**35.3, 50.4**
		Secular trend β1	–0.06	0.2	0.8	–0.5, 0.4
		Change in level β2	5.0	6.0	0.4	–7.3, 17.6
		Change in trend β3	1.7	1.6	0.3	–1.5, 4.9
(f)	% of antibiotic prophylaxis duration>24h	Constant β0	**95.6**	**1.1**	**0.000**	**93.4, 97.8**
		Secular trend β1	**–0.8**	**0.07**	**0.000**	**–0.9, –0.7**
		Change in level β2	**–8.6**	**2.6**	**0.003**	**–13.9,–3.3**
		Change in trend β3	**–2.2**	**0.6**	**0.002**	**–3.4, –0.9**

SE, standard error; CI, confidence interval; OP, outpatient; IP, inpatient.

Notes:

a β0 is the intercept of the pre-intervention trend line (value of the variable at the start of the observation); β1 is the slope of the pre-intervention trend line (the baseline trend); β2 is the immediate post-intervention absolute change (immediate

effect of the intervention); β3 is the change of the post-intervention trend; and β1 + β3 is the slope of the post-intervention trend line.

b Bold signifies statistically significant coefficient (P < 0.05).

We found that the patterns of IP consumption of different categories of antibiotics were quite different between Chinese and Swedish hospitals. In Chinese hospitals, IP consumption of antibiotics for systemic use (J01) sharply dropped from 819 DDD/1 000 inpatient days in 2010 to

Table 2 Comparison of antibiotic use patterns and consumption pressure in Chinese public general tertiary hospitals with the Chinese national targets and the Swedish levels in 2012

Outcome measures		15 Chinese public general tertiary hospitals	Chinese national targets[a]	Seven Swedish university hospitals
(a)	Proportion of OP[1] prescriptions with antibiotics	10% (n=18,000, SD=1.14,95% CI [7.96%, 12.83%])	<20%	1.1%[b,c]
(b)	Proportion of OP[1] prescriptions with parenteral antibiotics	2% (n=18,000, SD=0.55,95% CI [0.99%, 3.34%])	NA	0.001%[c]
(c)	Proportion of IP[1] medical records with antibiotics	50% (n=5,400, SD=2.0,95% CI [37.96%, 64.17%])	<60%	34%[d]
(d)	Proportion of IP[1] medical records with parenteral antibiotics	46% (n=5,400, SD=1.96,95% CI [42.26%, 50.67%])	NA	15%[d]
(e)	Proportion of antibiotic prophylaxis before incision	55% (n=1,708, SD=7.51,95% CI [39.29%,71.51%])	100% (except cesarean)	NA
(f)	Proportion of antibiotic prophylaxis duration>24h	56% (n=1,708, SD=8.11,95% CI [38.5%, 73.28%])	Generally<24h (except specific conditions)	33%[d]
(g)	Total IP consumption of antibiotics for systematic use (J01)	473 DDD/1,000 inpatient days (n=15, SD=28.96, Median=464.43)	<400	588 DDD/1,000 inpatient days[c]
	IP Consumption of penicillins (J01C)	51 DDD/1,000 inpatient days (10.82% of J01) (n=15, SD=7.68, Median=40.00)	NA	263 DDD/1,000 inpatient days[c] (44.73% of J01)
	IP Consumption of quinolones (J01M)	51 DDD/1,000 inpatient days (n=15, SD=6.05, Median=47.93)	NA	58 DDD/1,000 inpatient days[c]
	IP Consumption of 1st generation cephalosporins (J01DB)	44 DDD/1,000 inpatient days (n=15, SD=4.92, Median=44.75)	NA	5 DDD/1,000 inpatient days[c]
	IP Consumption of 2nd generation cephalosporins (J01DC)	82 DDD/1,000 inpatient days (n=15, SD=8.07, Median=73.74)	NA	13 DDD/1,000 inpatient days[c]
	IP Consumption of 3rd generation cephalosporins (J01DD)	105 DDD/1,000 inpatient days (22.24% of J01) (n=15 hospitals, SD=14.72, Median=93.91)	NA	53 DDD/1,000 inpatient days[c] (9.01% of J01)
	IP Consumption of 4th generation cephalosporins (J01DE)	19DDD/1,000 inpatient days (n=15, SD=5.11, Median=16.96)	NA	0[c]

OP, outpatient; IP, inpatient; S.D., standard deviation; CI, confidence interval; N/A, not available (no specific target); DDD, defined daily doses.

Notes:

a Ministry of Health of P.R China.

b In DDD.

c 2012 sales data.

d 2010 Swedish Strategic Programme against Antibiotic Resistance (STRAMA) point prevalence survey data.

473 in 2012. Table 2 shows that in 2012, the IP consumption of third-generation of cephalosporins (J01DD) reached 105 DDD/1 000 inpatient days (22.2% of J01), while that of the penicillins (J01C) was 51 DDD/1 000 inpatient day (10.8% of J01). Conversely, in Swedish hospitals, IP consumption of all these categories were stable throughout 2005–2012, ranging between 572 and 645 DDD/1 000 inpatient days. J01C was the major antibiotic group consumed during 2005–2012, with an IP consumption of 263 DDD/1 000 inpatient days in 2012 (44.7% of J01), while that of J01DD was only 55 DDD/1 000 inpatient days (9.0% of J01) (Table 2).

DISCUSSION

Changes in antibiotic use in Chinese hospitals before and after the introduction of the 2011 interventions

From the outcome indicators of antibiotic use (a–f), we found that antibiotic prescription in Chinese hospitals was falling before the 2011 interventions. The segmented regression analysis also confirmed this finding. An explanation may be that the Ministry of Health had issued a series of regulations since 2002, which will have probably had an impact. The regulations included the requirement to establish a hospital Drug and Therapeutics Committee in 2002,[20] strengthened regulations on prescriptions,[21] guidelines for antimicrobial use in 2004,[22] the establishment of a use and resistance monitoring network in 2005,[23] improving antibiotic prophylaxis for surgery in 2008 and 2009 and developing guidelines for prescription audits in 2010.[24]

Although the 2011 interventions effected immediate and significant reductions in antimicrobial use, we could not conclude that the effects were solely caused by the 2011 interventions, because these indicators already had significantly decreased baseline trends.

Using the internationally recognized standard for comparative drug utilization research (ATC/DDD systems), we found more subtle trends in indicator g. The IP consumption of antibiotics for systemic use (J01) decreased in 2008 and further decreased following the 2011 interventions. Until December 2012, it quickly dropped to almost one-half of the highest level. Broad-spectrum antibiotics always dominated prescribing during 2005–2012, and reached a peak in 2012. Conversely, the consumption of narrow-spectrum antibiotics continuously decreased during 2005–2012.

Comparison of antibiotic use in Chinese and Swedish hospitals

IP antibiotic consumption of Swedish hospitals has been well controlled at a stable level over time and, like most of other EU countries, penicillins (J01C) are always the most frequently used antibiotics.[25] In contrast, IP antibiotic consumption in Chinese hospitals dropped sharply from an unacceptably high level to the equivalent to the 2012 Swedish level. The absolute values of each studied ATC category all decreased. The proportion of the third-generation of cephalosporins (J01DD) prescribed to all prescribed antibiotics for systemic use (J01) did not change and it was the dominant class, whereas

penicillins (J01C) fell throughout the period.
The significant reductions in OP and IP antibiotic do not address the more appropriate use. However, there are achievements measured against a background of an unacceptable baseline. Even though the proportions of OP & IP antibiotic use achieved the national targets following the 2011 interventions (there were no targets for parenteral antibiotics use), antibiotic prophylaxis usage and practice still falls short of the national targets as well as Swedish usage.

It is concerning that Chinese hospitals still use more broad-spectrum antibiotics than narrow-spectrum antibiotics, and that such preferences did not change. Broad-spectrum antibiotics have been generally regarded by many Chinese doctors and the general public as the more efficient treatment to address all kinds of infections. There is also a reluctance to use diagnostics and a heavy reliance on empirical treatment. The second factor is that the Chinese guideline requires allergy test for penicillins (excluding a few oral formulations).[26] Chinese doctors tend to avoid skin testing procedures and are averse to any potential risk of dispute with the patient due to allergy, which contrasts with most other countries where a negative allergy history is accepted" Resistance rates in China are much higher than Sweden and prescribers believe immediate use of broad-spectrum agents give the best empirical cover. Greater availability of resistance data should encourage the use of narrow-spectrum agents.

Although overuse of antibiotics had been reduced in Chinese hospitals through the joint efforts during 2002-2011, the Chinese national targets are yet to be met and there is a significant gap compared with Swedish hospitals. The primary care system in China was not as effective as in Sweden, particularly for patient referred to hospital. Despite efforts to build the capacity in the primary care in China, patients still prefer to directly seek hospital care due to a lack of trust, no compulsory referral mechanism, and a weak referral capacity in primary care. Approximately 60% of the medicines market is dominated by tertiary hospitals in China,[27,28] and Chinese patients will always go directly to tertiary hospitals for common diseases. In Sweden, primary care forms the foundation of the healthcare system. Although there is no formal gate-keeping role for primary care in most county councils, it plays an important role in guiding the patient to the right care within the health system.[2,11] It might be inferred that Chinese patients require less intensive antibiotic treatment than the patients in the equivalent Swedish settings, which should lead to a lower consumption in China. Alternatively, Swedish IP consumption data were collected from the sales data, which might be higher than the data collected from medicines procurement and inventory management systems leading to the apparent anomaly.

Chinese and Swedish hospitals have opposing trends for the use of narrow-and broad-spectrum antibiotics but similar IP antibiotic (for systemic use) consumption. Such a contradiction could be explained by the 2011 interventions causing a rapid significant reduction in overall antibiotic consumption. The high rate of antibiotic use might be due to unnecessary treatment of minor illnesses and non-bacterial infections, combined with under-treating serious bacterial infections due to tight restrictions on antibiotic use. Further studies are needed in China to investigate guideline compliance

and hospital-acquired infection rates. In addition, as our consumption measurement does not include OP and community pharmacies, we do not know if IP antibiotic use was shifted to OP or over-the-counter sales.

Another reason should be considered is that, the Chinese longitudinal data of antibiotic use indicators (a–f) might be an underestimate as they did not include data from departments with a potential high use (e.g. infectious diseases).

Ideally, we would have used the existing Chinese national monitoring network data to conduct this study. However, due to the unavailability of the national data, we had to conduct a sampling study whilst social, demographic, and economic characteristics of different geographic areas were considered in selecting hospitals. The hospitals were all part of a special national monitoring network and may be atypical.

The internationally recognized DDD/ATC system was used in our comparisons of patterns of antibiotic use between China and Sweden. However, the Chinese medicines classification system is different from the ATC system, and different prescribed doses are used in different countries. We only targeted the antibiotic categories that were similar between the Chinese system and ATC system to attempt to reduce this bias.

There are also some limitations in the Swedish data. Unlike the IP consumption data collected in China, we extracted sales data of antibiotics to the hospital wards were extracted, but not what was actually used by the patients. This may result in an overestimate of antibiotic use in Sweden. In addition, due to the limitation of Swedish data availability (consumption data only in 2009-2012, IP antibiotics use only in 2010), these do not exactly match with the years of the Chinese data (consumption data in 2005-2012, IP antibiotics use data in 2012).

Segmented regression analysis of interrupted time series data is the strongest, quasi-experimental design to evaluate longitudinal effects of time-delimited interventions. This evidence would be stronger if a control setting was available. Due to the restriction of data availability, we were not able to obtain control data.

Data from our study do not enable us to understand whether the changes in China have resulted in less inappropriate antibiotic use, or whether antibiotics use has been shifted from IP to other sources. Some intervention strategies lsuch as "revoking prescription rights of the frequent outliers" may lead to that appropriate antibiotic use being denied. Sophisticated policies are needed to guide antibiotic use rather than simple restriction of use. There is also a clear need to obtain better surveillance of both antibiotic resistance and usage to guide future interventions.

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Chapter 4

The Effects of Key Health System Reform Policies on Medicines

4.1 The Effect of Implementing "Medicines Zero Mark–up Policy" in Beijing Community Health Facilities

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ABSTRACT

The "medicines zero mark-up policy" was introduced in Beijing community health centers (CHCs) with three government subsidy approaches: fixed subsidy (FS), income-linked subsidy (IS) with income and expenditure controlled by government, and self-financing with mark-up compensation from government procurement services (GPS). This study analyzes the cost containment effect and its effect on the operation of CHCs and staff morale. CHCs are randomly selected and distributed in three government subsidy approach groups. The effect was measured with changes of medicines use & cost, income of facilities and staff before and after the policy in each group, and compared among groups. Cost proportion of "zero mark-up" medicines per visit in FS/IS/GPS was 75.4%/57.8%/52.6% by 2009. The medicines costs per visit in FS and IS groups reduced 18.7% and 1.9% respectively by the end of first implementation year in 2007, and rebounded in 2008 and 2009. Both reductions were with statistical significance ($p=0.001$, $\alpha=0.05$, t-test). There was a significant difference between the reductions of medicines cost per visit between FS and IS groups ($p=0.016$, $\alpha=0.05$, t-test). GPS increased 25.2% by 2007 and kept growing. Between 2006 and 2009, government subsidy was always the highest in FS and lowest in GPS. The annual salary of FS was always the highest and increases the fastest. The "medicines zero mark-up policy"contained medicines costs. FS was more effective than IS and GPS. GPS caused lower willingness to use "zero mark-up" medicines. FS and IS had to improve the work enthusiasm of the staff. IS had the mixed effect.

BACKGROUND

During the planned economy, free medical services were provided to everyone in China. Public health facilities heavily relied on government subsidies and the government set a price which was far below real costs. Medicines mark-up by public health facilities was first allowed in 1954, when the Chinese economy experienced the most difficult times.[1] Such a policy gradually evolved into a perverse incentive along with the economic reform starting from 1978, when public health facilities were encouraged to generate revenues and were allowed to issue bonuses. In turn, the income of individual staff was directly linked with revenue generation. The unchanged low level medical service fee forced providers to generate more revenue from mark-up of medicines. This contributed to unnecessary prescriptions written by doctors. Doctors preferred expensive medicines and poly-pharmacy, which contributed to increased medical cost and public out-of-pocket expenditure.[2]

Beijing implemented the "medicines zero mark-up policy" in the community health centers (CHCs) in 2007. The aims of the policy were to eradicate the afore-mentioned incentives, contain the medicines cost, and reduce the financial burden to the public.[3] Policy-makers selected 312 medicines based on the national essential medicines list. The CHCs were required to procure these medicines via government pooled tendering. Procurement and prescribing of "non zero mark-up" medicines were allowed and the CHCs were to dispense these medicines at the procurement price.[4] Government subsidized CHCs via three financial approaches: (1) in high socioeconomic districts, the government allocated fixed subsidies (FS) to CHCs and all expenditures of CHCs were secured according to defined standards. Even in areas of deficit, the government subsidy was still allocated to CHCs. No surplus was allowed to be retained by individual CHCs; (2) in the poorer districts, the government allocated income-linked subsidy (IS), covering only staff and not other operational costs. The amount of subsidy was related to revenue generated; (3) for a few specific CHCs, the government did not bear their operational costs, but purchased services (GPS) from them, i.e. compensated the mark-up loss from selling "zero mark-up" medicines based on their historical medicines sales. These CHCs were responsible for balancing expenditure against revenue and had the autonomy to retain any surplus.[5,6]

There are a number of studies which have analyzed the changes of medicines cost for patients in specific facilities after implementation of this policy in Beijing.[7-10] Li's regression analysis model7 showed that the government subsidy approach was a very important factor towards total medicines cost. This study analyzes the effects of the "medicines zero mark-up policy" on medicines cost, the operation of CHCs, and the work enthusiasm of the CHC staff with different government subsidy approaches (GSA) in FS, IS and GPS groups.

Table 1 CHC sampling scope and distribution in each district of Beijing

				Fixed subsidy CHCs		Income-linked subsidy CHCs		Government purchase of services CHCs	
	Name of districts	Number of CHCs	Sample number	Number of CHCs	Sample number	Number of CHCs	Sample number	Number of CHCs	Sample number
	Total	**351**	**70**	**91**	**17**	**214**	**42**	**46**	**11**
Fixed subsidy districts	Dongcheng	40	6	40	6	0	0	0	0
	Xuanwu	8	2	8	2	0	0	0	0
	Chongwen	5	2	5	2	0	0	0	0
	Yanqing	15	3	15	3	0	0	0	0
	Sub-total	**68**	**13**	**68**	**13**	**0**	**0**	**0**	**0**
Fixed subsidy & government purchase of services districts	Fangshan	24	4	23	4	0	0	1	0
	Sub-total	**24**	**4**	**23**	**4**	**0**	**0**	**1**	**0**
Income-linked subsidy & government purchase of services districts	Xicheng	7	3	0	0	6	3	1	0
	Chaoyang	42	6	0	0	34	4	8	2
	Fengtai	23	4	0	0	13	2	9	2
	Shijingshan	8	4	0	0	2	2	7	2
	Haidian	26	6	0	0	20	4	6	2
	Mentougou	11	4	0	0	9	2	2	1
	Tongzhou	30	4	0	0	19	3	11	2
	Shunyi	25	5	0	0	24	5	1	0
	Sub-total	**172**	**36**	**0**	**0**	**127**	**25**	**45**	**11**
Fixed subsidy districts	Changping	15	3	0	0	15	3	0	0
	Daxing	20	4	0	0	20	4	0	0
	Huairou	16	3	0	0	16	3	0	0
	Pinggu	18	4	0	0	18	4	0	0
	Miyun	18	3	0	0	18	3	0	0
	Sub-total	**87**	**17**	**0**	**0**	**87**	**17**	**0**	**0**

METHODS

Utilization of "zero mark-up" medicines, medicines costs per visit, government subsidy, medicines and medical revenue of CHCs, and CHC staff salaries were measured before the introduction of the "medicines zero mark-up policy"in 2006 and then three years following implementation of the policy. We divided the CHCs into three groups according to GSA and compared the changes of the above measurements among three CHCs group with different subsidy approaches (FS, IS and GPS). We randomly selected 20% of the total number of CHCs adopting the same GSA in each district[11] (Table 1). All data were directly obtained from a health information database of the CHCs.

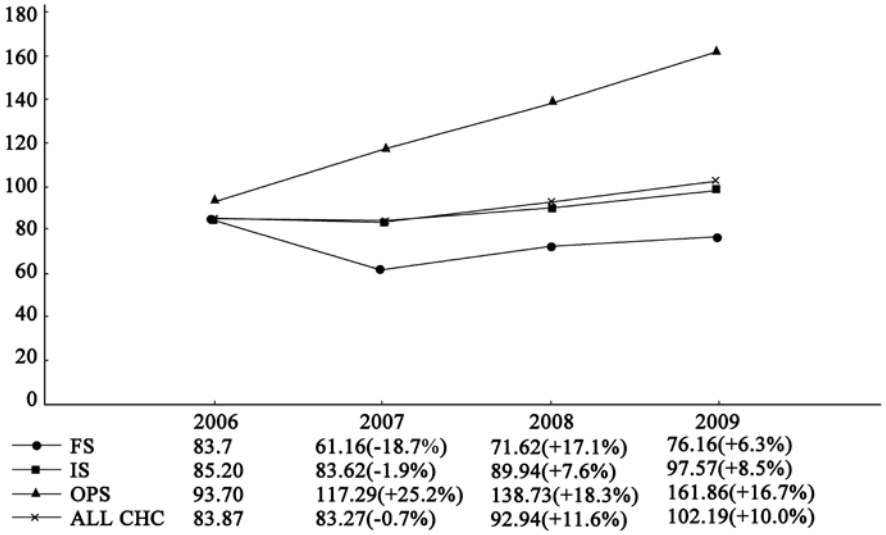
A paired t-test was conducted to test the differences of medicines cost per visit one year before and after the implementation of the "medicines zero mark-up" policy in both FS and IS groups. A t-test for two independent samples (FS and IS groups) was conducted to compare the difference of the above policy impact on medicines cost per visit between 2006 and 2007 between FS and IS groups. As the primary cost data are not normally distributed, a natural logarithmic transformation was undertaken in order to normalize the data. Statistical analysis was undertaken using by SPSS® version 17.0.

RESULTS

The proportion of "zero mark-up" medicines cost to total medicines cost per visit quickly increased in all CHCs in 2007, maintained in 2008-2009, and achieved in 75.4%, 57.8%, and 52.6% in the fixed subsidy, income-linked subsidy and government purchase of services facilities respectively. CHCs with fixed subsidies demonstrate greater willingness to use "zero mark-up" medicines.

The medicines costs per visit in FS and IS groups reduced 18.7% and 1.9% respectively by the end of first implementation year in 2007, and rebounded in 2008 and 2009. Both reductions were with statistical significance (P=0.001, α=0.05). There was a significant difference between the reductions of medicines cost per visit between FS and IS groups (p=0.016, α=0.05). The medicines cost per visit in government purchase of services facilities increased 25.2% in 2007, and kept growing during 2008-2009, which is in line with the results of other studies conducted in recent years[7-10](Fig. 1).

Fig. 1 Medicines cost per visit in 70 sample CHCs during 2006-2009(CNY)

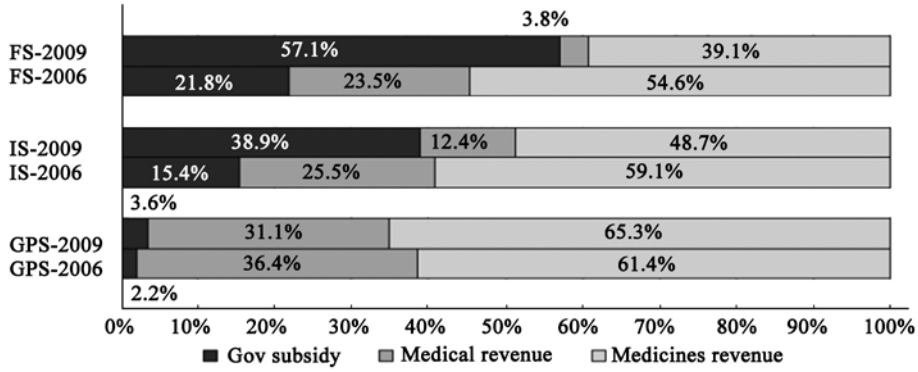


Abbreviations:

CHC means community health center; FS means fixed subsidy; IS means income linked subsidy; OPS means government purchasing services.

Government subsidy to CHCs with different GSA all increased during 2006-2009. Such increase was a general trend around the country during the same time. FS group was always the highest and GPS group grew the slowest all along 2006-2009. The proportion of government subsidy to the total revenue grew the fastest in FS group from 21.8% to 57.1%. GPS group grew the slowest from 2.2% to 3.6%. IS group was in the middle (grew from 15.4% to 38.9%). The proportion of medical and medicines revenue shrunk both FS (from 23.5% to 3.8%, and from 54.6% to 39.1%), and IS groups (from 25.5% to 12.4%, and from 59.1% to 48.7%). GPS group generated more medicines revenue (from 61.4% to 65.3%), but less medical revenue (from 36.4% to 31.3%) during 2006-2009. GPS group always generated the highest total (medicines and medical) revenue. It kept at a continuing growth rate of 20.3%, 23.3% and 22.1% during 2006-2009 in GPS facilities, while FS and IS groups generated less total revenue (26.3% and 5.3% less) by the end of the first implementation year of 2007. Even though it turned to increase in 2008 and 2009 in FS and IS groups, the total revenues in FS and IS group were only about 20% and 30% of that in GPS group in 2009 (Fig.2).

Fig. 2 Proportion of government subsidy, medical & medicines revenue to the total income in 70 studied CHCs



Abbreviations:
CHC means community health center; FS means fixed subsidy; IS means income linked subsidy; OPS means government purchasing services.

The annual staff salary in all CHCs continued to rise during 2006-2009. Wang's study[9] showed the same increasing trend of CHC staff salary in Beijing in 2007-2008. Facilities were government purchased services always had the lowest staff salary. Income-linked subsidy facilities consistently had the highest staff salary costs.

DISCUSSION

At the initial stage of the policy implementation, CHCs were allowed to procure "non-zero mark-up" medicines. Although the Beijing Health Bureau primarily expected that, the "zero mark-up" medicines list would be able to meet the majority medicines needs in CHC. In reality, the range of medicines actually used in all CHCs was beyond that list. The list was then expanded in the following years step by step with the growing economy and the affordability. There has been a challenge for selection of the most cost-effective medicines within the limited financial capacity of the society, the government, and individuals.

Fixed subsidy group was more willing to adopt "zero mark-up" medicines than IS and GPS groups, which is probably due to that they receive full financial support from the government and therefore they have reduced financial pressures. These CHCs have no autonomy to keep any surplus generated and so there is neither incentive for them to generate more revenue nor incentive to procure medicines outside the essential medicines list. In the facilities where governments purchase services, budgets are not controlled by the government and so these CHCs have a strong incentive to generate revenue. These CHCs mat prefer "non zero mark-up" medicines in order to generate more medicines revenue. Income-linked subsidy facilities can potentially generate more revenue by requesting a greater level of government subsidy. Budget management may help to restrain such intentions, so these CHCs have moderate incentive to prescribe "non zero mark-up" medicines.

Such "incentive" and "absence of incentive" also affect the other aspects of performance. Medicines costs were better contained as there was no revenue generation pressure in the fixed subsidy facilities. With the revenue generation incentive and a loosed control on medicines use, the government purchase of service facility would pursue the maximum of both quantity and unit service price. On one hand these CHCs try their best to attract more patients and provide more services, on the other hand these facilities would prescribe more medicines (either "zero mark-up" or "non zero mark-up" medicines) in-order to request greater government subsidy or to earn a higher level of more mark-up.

The result regarding levels of staffing salaries warrants consideration. It is assumed that with increased revenue the CHCs supported through government purchase of services should have higher salaries but this study suggests the contrary. It is possible that these CHCs did not disclose full income data so as not to affect future requests for subsidies from the government. This type of CHC is very likely to have un-official bonuses to stimulate and maintain enthusiasm for work. Salary scales in fixed subsidy facilities were significantly improved following the introduction of the "medicines zero mark-up policy "with the security of full government subsidy being in place.

CONCLUSION

The "medicines zero mark-up policy "did help in containing the rising trend in costs of medicines. The medicines cost per visit was significantly reduced one year post the policy implementation. Fixed subsidy approach was found to be more effective in reducing financial burden of medicines for patients.

LIMITATIONS

There are several limitations of this study and the results need to be considered with respect to these. Firstly, data were obtained from randomly selected CHCs, and factors such as facility scale and operation status were not considered. This may not fully reflect every specific aspects of the effect of policy. Second, in responding to the inflated costs in 2008 and 2009, the study did not involve in-depth key informant interviews to explore the reasons behind this and whether it was provider driven or demand driven. The assumption is made that a more comprehensive and consistent medicines use regulation is needed. No in-depth analysis of the contributors (changes of number of visits and quantity of medicines per prescription) to the differences in medicines and medical revenue generated by facilities was undertaken. Further, the study does not evaluate whether the quality of care provided by these facilities is affected by this policy and there is no understanding of the levels of satisfaction of the public and CHC staff. This is a rich area of future research and the current study provides a platform for doing more.

ACKNOWLEDGMENT

We thank the Beijing Health Bureau for approving this study and supporting the field survey and data collection.

AUTHOR CONTRIBUTIONS

The order of the authors of this manuscript follows the original project report. Considering that the other authors are the key recipient of the project fund, Jing Sun is only listed as the 4th author of this manuscript. In fact, Jing Sun provided major contribution to the conception and design of this evaluation study and data interpretation, and the manuscript was drafted and critically revised by Jing Sun. She is also the corresponding author.

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Chapter 4

The Effects of Key Health System Reform Policies on Medicines

4.2 Did the Capitation Payment Reform Make a Difference for Primary Care in China?

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Weibin Zhang
Yongqian Tan
Weixian Xiang

Healthcare in Low–resource Settings 2014; 2:1839p9–13

ABSTRACT

Shifting fee-for-service to capitated payment to primary health providers has been regarded as a tool of insurance programs to contain costs and to change prescription behaviors in China. This paper explored if such a reform achieved its expected objectives in rural primary healthcare in Qianjiang, a less developed county in west China. Key measurements included cost, prescription behaviours, hospitalization and referral rate, and provider income. Retrospective administrative claims were analyzed to compare changes of these measurements in the studied facilities started the reform in different stages, and to compare with overall Qianjiang. Growth rate of cost was contained at the beginning of each stage of reform. The containment effect vanished thereafter. Except a significant increase of the proportion of number of essential medicines to total medicines per prescription in township health centers, prescription behaviors were not significantly improved. No significant change of referral rate was observed. Hospitalization rate shifted from upward to downward after the reform. Monthly income and outpatient revenue continuously increased. To conclude, the capitated payment reform in Qianjiang achieved cost containment objective without unintended results, but failed to achieve prescription behavior change objective. More comprehensive combined policies are needed.

INTRODUCTION

After the foundation of the P.R.China, health security system for rural residents relied on a collective model under the planned economy.[1] In 1978, this health security system collapsed when China shifted from the planned economy to the market economy.[2] In 2003, New Rural Cooperative Medical Scheme (NRCMS) was set up to provide basic health security for rural residents. It greatly alleviated the medical needs of farmers constrained in a longtime since 1978. The financing of NRCMS heavily relies on government subsidy. NRCMC expenditures have been continuously increasing, due to rapid progress towards universal population coverage and significant improvements of benefit packages. The governments have increasing cost containment pressures to keep the financial sustainability of NRCMS. [3]

Fee-for-service (FFS) is the key payment method of NRCMS. Intermixed with other complicated factors (including distorted pricing policies, policies allowing hospitals to generate operational fund from selling medicines through dominated hospital pharmacies, etc.), FFS has been creating perverse incentives in Chinese health systems, driving preference of expensive medicines and over prescriptions, and intensifying the surging medical costs.[4,5]

International experiences also demonstrated the inefficiency of FFS payment, and its problematic financial incentives for overuse of services. It does nothing to encourage cost-effective services and thus lower the value of care.[6] Paying physicians with FFS is the major driver of higher health care costs in the United States, which is a country with the highest health expenditure in the world.[7,8]

There have been increasing numbers of high and low income countries looking to capitated payment to avoid the cost inflation effect of FFS payment.[9-13] Many Chinese local insurance programs also piloted capitated payment reforms.[14,15] Qianjiang is one of the case. NRCMS in Qianjiang shifted its payment to the designated primary health facilities from resource exhausted FFS to capitation in July 2007. The expected aims were to encourage cost-effective care through raising cost awareness of providers with capitated payment to providers, thereby to contain the surging NRCMS expenditures.[16]

As most of the existing studies about capitated payment in China only documented its effects on cost, little was studied on prescription behaviors and health outcomes.[17] This paper comprehensively measured if the capitated payment reform made any changes to the rural primary healthcare in Qianjiang in the full aspects: cost containment, changing prescription behaviors, altering referral and hospitalization rates, and affecting provider income. It ended by identifying lessons for better implementation of this reform.

MATERIALS AND METHODS

Township health centers and village clinics are the key primary health providers in rural China. The capitated payment reform in Qianjiang targeted the outpatient services of township heath centers and village clinics.

Reform started in two village clinics in July 2007. Another 49 village clinics followed in January 2008. All 158 village clinics and four township health centers joint in October 2008. The reform expanded to all primary health facilities including 158 village clinics and 30 township health centers in January 2009.

To measure the effect of the reforms in four phases, we randomly selected six village clinics and three township health centers as studied facilities. The sample size was determined to have at least 10% of 51 village clinics and four township health centers in initial phase I and II reforms.[17] Reform implementation and sampling flowchart was described as showed in Table 1.

Table 1 Capitated payment reform implementation in Qianjiang and the studied facilities selection flowchart

Reform phase	Reform time	Facilities in each phase of reform	Reform group	Sample size
Phase I	July 2007	2/158 village clinics	1st Group	2 village clinics
Phase II	Jan. 2008	51/158 village clinics	2nd Group	4 village clinics
Phase III	Oct. 2008	158 village clinics + 4/30 township health centers	3rd Group	3 township healthcenters
Phase IV	Jan. 2009	158 village clinics + 30 township health centers	/	/

Cost, prescription behaviors, outpatient & inpatient services utilization, and provider income were the key measurements, which were listed in Table 2.

Annual average total costs per visits were calculated based on the data directly extracted from Qianjiang NRCMS management database. The change of it during 2006-2009 was compared among different groups of the studied facilities started the reform in different phases, and compared with overall Qianjiang, as well as with the maximum expenditure per prescription (major components of outpatient service cost are for medicines). The changes of proportion of essential medicines prescribed, proportion of prescriptions with antibiotics, steroids and injectables/infusions were measured to assess the prescription behavior. The

Table 2 Key measurements

Reform effects	Measurements
Cost containment	Annual average total cost per visit (CNY)
	Maximum expenditure per prescription (CNY)
Prescription behavior	% of prescriptions with antibiotics
	% of prescriptions with steroids
	% of prescriptions with injectables/infusions
	% of essential medicines prescribed
Outpatient service	Referral rate (%)
Inpatient service	Hospitalization rate (%)
Provider income	Facility monthly revenue (CNY)
	Staff monthly salary (CNY)

change of referral rate helped to assess if patient selection occurred. Hospitalization The change of hospitalization rate reflected if patients were shifted from outpatient to inpatient care. The change of revenue of facilities and salary of staff showed if the interests of primary health providers were affected by the reform. Prescription and income data was obtained from surveys in the studied facilities. Under the support of Qianjiang Health Bureau, the studied facilities were required to track prescriptions, and reported income and revenue. Referral and hospitalization rates were regular data collected annually, which were extracted from the Qianjiang NRCMS management database. Township health centers and village clinics were compared separately.

RESULTS

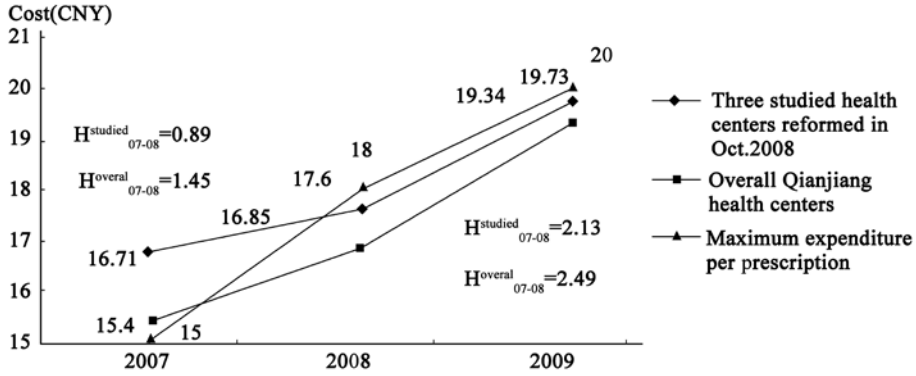
Annual average total cost per visit

Township health centers (Fig. 1)

In 2007, no township health centers started the reform. The annual average total cost per visit of three studied township health centers (CNY 16.71, US$ 2.3, exchange rate=7.3) and that of overall Qianjiang township health centers (CNY 15.4) were above the 2007 maximum expenditure per prescription (CNY 15).

Reform started in four township health centers in October 2008. The annual average total cost per visit of three studied township health centers reached CNY 17.6. The annual average cost per visit of overall Qianjaing township health centers reached CNY 16.85. Both increased, but were still under the 2008 maximum expenditure per prescription (CNY 18). The intercept of three studied township health centers was smaller than that of overall township health centers between 2007 and 2008: $H^{studied}_{07\text{-}08}(0.89) < H^{overall}_{07\text{-}08}(1.45)$. Assumed that the contribution of three studied facilities (changes brought by the capitated payment reform started in October 2008)

Fig. 1 Annual average total cost per visit of health centers 2007-2009



Source:NRCMS management database of Qianjiang Health Bureau

to 30 overall facilities in 2008 could be neglected. Although the capitated payment reform only implemented three months in 2008, it still gained cost containment effect, as the growth rate of annual average cost per visit got smaller.

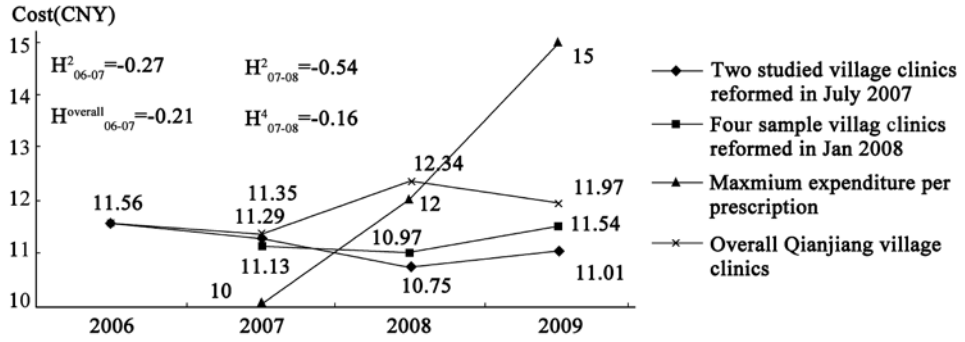
The other 26 township health centers joint the reform in January 2009. The annual average total cost per visit of three studied township health centers (CNY19.73) and overall Qianjiang township health centers (CNY19.34) further increased in 2009. The growth rate of the latter one was faster than that of the former one. Both went below the maximum expenditure per prescription (CNY 20). The intercepts of three studied and overall township health centers between 2008 and 2009 were: $H^{overall}_{08-09}$=2.45 and $H^{studied}_{08-09}$=2.13. $H^{overall}_{08-09}>H^{studied}_{08-09}>H^{overall}_{07-08}>H^{studied}_{07-08}$, which implied that: (1) in 2009, the growth rate of annual average cost per visit of overall Qianjiang township health centers was faster than that of the three studied township health centers which joined the reform in October 2008. No cost containment effect was observed of the capitated payment reform started in January 2009; (2) the growth rate of annual average cost per visit in three studied township health centers in 2009 was faster than that in overall Qianjiang township health centers in 2008. Cost containment effect in 2008 on three studied township health centers did not continue in 2009.

Village clinics (Fig. 2)

Annual average cost per visit of two studied village clinics in 2006 was not available. Assumed that there was no significant difference among the two studied village clinics started the reform in July 2007, the four studied village clinics started the reform in January 2008, and the other village clinics before implementation of the capitated payment reform. Also assumed that, the contribution brought by two studied village clinics to 158 overall village clinics in July 2007 could be neglected. Annual average

cost per visit of overall Qianjiang village clinics in 2006 (CNY 11.56) was regarded as the baseline of the 1st group (two studied village clinics pioneered the reform in July 2007) and the 2nd group (four studied village clinics joined the reform in January 2008) village clinics. The annual average total cost per visit of two studied village clinics (CNY 11.29) was a bit lower than that of overall Qianjiang village clinics (CNY 11.35) in 2007. Both decreased and were above the maximum expenditure per prescription (CNY 10). Larger intercept of two studied village clinics between 2006 and 2007 ($H^{2}_{06\text{-}07}$= -0.27) than that of overall village clinics ($H^{overall}_{06\text{-}07}$= -0.21) in the negative part of Y-axis, implied slight cost containment effect in 2007 on two studied village clinics.

Fig. 2 Annual average total cost per visit of village clinics 2006-2009



Source:NRCMS management database of Chongqing Health Bureau

In January 2008, another 49 village clinics jointed the reform. Annual average total cost per visit of two and four studied village clinics decreased to CNY 10.75 and 10.97 respectively. Both were lower than the maximum expenditure per prescription (CNY 12). On the contrary, that of overall village clinics further increased to CNY 12.34. This indicated that, cost containment effect of the capitated payment reform in July 2007 on the 1st group of two studied village clinics continued in 2008, and there was also positive cost containment effect of the capitated payment reform in January 2008 on the 2nd group of four studied village clinics. The intercepts of two and four studied village clinics 2007-2008 were: $H^{2}_{07\text{-}08}$= -0.54 and $H^{4}_{07\text{-}08}$= -0.16. $H^{2}_{07\text{-}08}$-$H^{2}_{06\text{-}07}$=$H^{2}_{06\text{-}07}$<$H^{4}_{07\text{-}08}$ indicated that: (1) cost containment effect in 2008 on the 1st group of two studied village clinics kept same as it was in 2007; (2) cost containment effect in 2008 on the 2nd group of four studied village clinics was not as strong as on the 1st group of two studied village clinics.

In January 2009, all 158 village clinics fully implemented the capitated payment reform. The annual average total cost per visit of all village clinics shifted from upward to downward trend, and decreased to CNY 11.97. On the contrary, that of two and four studied village clinics increased to CNY 11.01 and 11.54 respectively. This indicated strong cost containment effects of the capitated payment reform in January 2009 on the 3rd group of village clinics. Cost containment

effects of the capitated payment reform in July 2007 on the 1st group of two village clinics, and cost containment effects of the capitated payment reform in January 2008 on the 2nd group of four village clinics did not continue.

Prescription behavior

During 2007-2009, the referral rates and prescription indictors of the studied township health centers were showed in Table 3. Statistic analysis showed that, the proportion of number of essential medicines to total medicines per prescription in the studied township health centers significantly increased following the reform (x^2test, $p<0.05$), that in the studied village clinics did not significantly change (x^2test, $p>0.05$). Other prescription indicators of the studied township health centers did not statistically change as well (x^2test, $p>0.05$). Steroids, antibiotics and injectables/infusions prescriptions in village clinics were not assessed due to absence of data. There was no significant change of referral rate following the reform.

Table 3 Prescription indictors and referral rates in sample facilities during 2007-2009

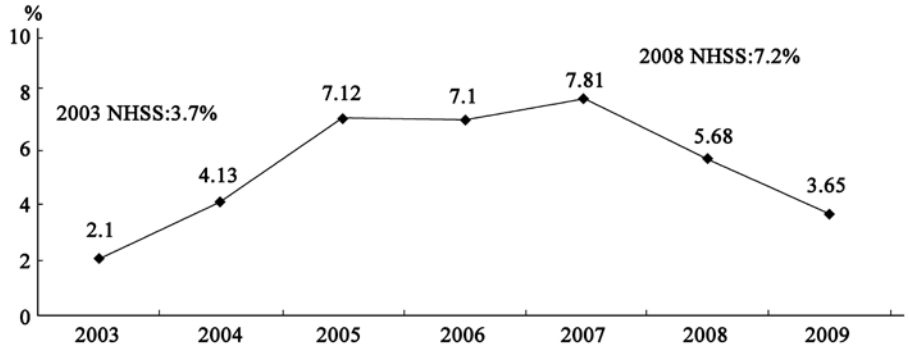
		2007	2008	2009	χ2	p
Referral rate in health centers (%)		37.16	36.45	36.24	0.018	0.8928
% of essential medicines	Health centers	95	100	100	7.6017	0.0058
	Village clinics	98	100	100	3.0101	0.0827
% of prescriptions with steroids in health centers		3.58	3.19	2.59	0.1616	0.6877
% of prescriptions with antibiotics in health centers		24.11	19.93	16.57	1.7573	0.185
% of prescriptions with injectable/infusions in health centers		13.69	12.92	11.90	0.1427	0.7056

Source: Qianjiang Health Bureau.

Hospitalization rate

Hospitalization rate of Qianjiang NRCMS enrollees was 2.1% in 2003, lower than the 2003 3rd National Health Service Survey (NHSS) age-standardized hospitalization rate in rural China (the low annual net per capita income group was 3.7%).[18] Hospitalization rate of Qianjiang NRCMS enrollees rapidly increased in the following four years. It continued the increase from 7.15 in 2006 to 7.81% in 2007. As only two village clinics piloted the capitated payment reform in 2007, they might not have any effect on the hospitalization rate of Qianjiang NRCMS enrollees. Following the expansion of the reform to another 49 village clinics in January 2008, and to the four township health centers in October 2008, hospitalization rate of Qianjiang NRCMS enrollees dropped to 5.68% in 2008. It was lower than the 2008 4th NHSS age-standardized hospitalization rate in rural China (the low annual net per capita income was 7.2%).[19] When all village clinics and all township health centers in Qianjiang joined the reform, hospitalization rate of Qianjiang NRCMS enrollees further dropped to 3.65% in 2009 (Fig. 3).

Fig. 3 Hospitalizations rates of Qianjiang NRCMS enrollees during 2003-2009 and 2003 3rd & 2008 4th NHSS age-standardized hospitalization rate in rural low annual net per capita income group



Source: Qianjiang Health Bureau.
Abb reviations: NRCMS means new rurual cooperative medical scheme;NHSS means nations health service survey.

Provider income

The monthly income of primary health facility staff in Qianjiang kept growing during 2007-2009. It increased from CNY 1,683 (US$ 231, exchange rate=7.3) to CNY 2,575 (US$ 379, exchange rate=6.8) in township health centers, and increased from CNY 1,220 to 1,975 in village clinics. The increasing government subsidies to primary healthcare during this period might contribute to the income growth the most. For example, the secured government subsidy to village doctors increased from CNY 500 per year in 2007 to CNY 2,160 per year in 2009.[20] The outpatient revenue of all studied facilities kept growing during 2007-2009. None of the studied facilities had actual expenditures that exceeded the capitated amount (Table 4).

Table 4 Salary, outpatient revenue and surplus of New Rural Cooperative Medical Scheme (NRCMS) fund in sample facilities 2007-2009 in CNY

	2007			2008			2009		
	Monthly income	Outpatient revenue	NRCMS outpatient fund surplus	Monthly income	Outpatient revenue	NRCMS outpatient fund surplus	Monthly income	Outpatient revenue	NRCMS outpatient fund surplus
Health centers	1,683	896,295	38,000	1,897	972,968	29,833	2,575	1,248,445	35,000
Village clinics	1,220	39,763	615	1,712	40,442	554	1,975	43,517	2,395

Source: Qianjiang Health Bureau

Discussion

Cost containment

Owing to the aging population and the rapid economic and medical technological development,

like in most of the other areas in China, total cost per visit in Qianjiang has been continuously growing. The capitated payment reform in Qianjiang did not decrease the cost, but contained its growth rate, and were kept below the maximum expenditure per prescription target.

The reform was implemented in four stages. All have cost containment effect on both village clinics and township health centers during the initial period in each stage of reform. Except that, the cost containment effect on the 1st group of two studied village clinics continued in 2008, it was not kept in all facilities in 2009. Such a phenomenon was caused by a shift of NRCMS management function from Health Bureau to the Insurance Bureau in 2009. Management and supervision were slacked in that year.

Prescription behavior

Although the proportion of number of essential medicines to total medicines per prescription in township health centers increased significantly, other prescription indicators did not significantly change. This was not a concrete demonstration of improvements. The reform did not have an overall significant effect on changing prescription behaviors. Prescription behaviors are complex and are affected by multiple perverse incentives like pricing system and others incentives in the health system, single capitated payment reform approach might not be able to make a complete change. Changing prescription behaviors will need more comprehensive interventions with combined multiple approaches.

Unintended patient selection

Unchanged referral rate implies that, under the capitated payment reform, prescribers did not simply reduce services, or select patients with minor illness to avoid comprehensive treatment. The reform did not bring un-intended side effect of patient selection,[21-24] which was successfully averted through a performance assessment system. A set of specific and comprehensive indicators were formulated with considerable weights to valued workload, revisit rate for the same symposium within 72 hours, etc. Quarterly and year-end evaluations were conducted. Irregular and spot checks were also carried out to examine performance. Payment was made monthly with 80% of the budgeted expenditure and settled at the year end. The final 20% payment could be full or 20% cut down, based on the results of various assessment results throughout the year, and was kept within the budget.[16,25]

Hospitalization rate

The rapid increasing trend of Qianjiang NRCMS enrollee hospitalization rate during 2003-2007 was in line with the observations on other areas.[26,27] NRCMS was initially designed to share the financial risks for hospitalization. Outpatient care was not reimbursable at the beginning stage. Enrollees had to be hospitalized in order to get reimbursed for some treatments. High hospitalization rate was thus induced. The expanded reform in all village clinics and four pioneer

township health centers in Qianjiang between January and October 2008 had a strong effect on reducing hospitalization rate of NRCMS enrollees. This could be explained by the positive incentive brought by the capitated payment, i.e. designated providers pronged to contract more outpatient patients in order to obtain more insurance fund. In addition, one supporting policy of the capitated payment reform was implemented in 2007, which imposed strict admission standard and strengthened supervision on inpatient services in NRCMS designated facilities. Hospitalization criteria were clearly defined and circulated to all NRCMS designated health facilities.[28] Unnecessary hospitalizations were regulated and possible shifts of patients from outpatient to inpatient services were controlled.

Provider income

The no overruns result and the continuously increased staff salary of township health centers and village clinics in Qianjiang showed that, maximum expenditure per prescription, insurance payment budget limit, and relevant supporting policies in inpatient services in Qianjiang were generally reasonable. These policies secured a steady implementation of the capitated payment reform. There was no negative impact on the operation of the facilities and the income of the health workers.

CONCLUSION

The cost containment objective of the capitated payment reform in Qianjiang was achieved, but needs strategy to keep sustainability. Prescription behaviors were partially improved with limited effects. More comprehensive interventions with combined multiple approaches are needed to change the complex prescription behaviors. Careful development of comprehensive performance assessment system and supporting policies were crucial to address the unintended effects of capitated payment, like patient selection and unnecessary hospitalization. The reform brought no financial loss to both the facilities and the individuals.

LIMITATIONS

Availability of data

In order to relief data collection workload, the study heavily relied on administrative data of Qianjiang Health Bureaus. Data was collected annually as an average, quarterly or monthly data was not available. The assessment was then a rough trend analysis rather than a strict interrupted time series analysis.

Quality of data

Data were obtained from Qianjiang Health Bureaus, and were reported by individual facilities. Although Chongqing and Qianjiang Health Bureaus organized regular trainings for lower

level health bureaus and facilities, helped them in conducting appropriate data collection and reporting, possible quality problems may still exist. We assumed that the reported data is true and correct.

Sampling

Reform started in two village clinics in July 2007, and expanded to all primary facilities of Qianjiang until January 2009. It was implemented in four stages within one and half year. It was difficult to design a good sampling model for concise measurement of the changes. Annual average data for Qianjiang covered facilities which reformed in different time period, which was contributed by the effects of reforms on different groups of facilities which started to reform in different time. Although the contributors were only a small number of facilities comparing with overall Qianjiang, its contribution was weak and could be neglected, 2007 and 2008 annual average data of overall Qianjiang village clinics was not a perfect controller for two pioneer village clinics and four studied village clinics. This was same for 2008 annual average data of overall Qianjiang township health centers, which was not a perfect controller for four pioneer township health centers.

Mixed policy effect

Although the payment reform was the most important reform in Qianjiang during 2006-2009, there were tremendous policy changes under the overall health system reform framework during the same period. Other policy changes might not directly link with the NRCMS payment, but might indirectly contribute to the effects either positively or negatively. The evaluation drew mixed effects of all those policy changes, among which the payment reform contributed the most. Comparison among different groups of facilities which reformed in different stages helped to control confounding policies effects.

Inflation factor

One of the key measurements of this study is cost, which was not adjusted by the consumer price index (CPI). CPIs for healthcare during 2006-2009 in the province where Qianjiang is located varied a little between 98.8 and 104.4. It included medical instrument, appliance and services, traditional medicines and western medicines.[29] The inflation effect to the cost containment analysis was neglected.

Patient care and facility indicator

Consultation time, dispensing time, patients' satisfaction, patients' perception on medicines use, and availability of key essential medicines are important indicators for comprehensive assessment on quality of care. However, they were not regularly collected and recorded in Qianjiang. This study did not include these patient care and facility indicators, instead of focused on prescribing indicators and referral rate. The aim was to focus analysis on prescribing behavior changes.

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Chapter 5

The Effects of Comprehensive and Integrated Health System Reform Policies on Medicines

5.1 Achieving Universal Health Coverage–the Case of Zhuhai City

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ABSTRACT

Universal health coverage cannot be achieved without evidence from research, which requires national and international support. We hope that our careful documentation of one of China's local experience in designing and implementing the basic health insurance coverage, and our analysis of how it helped to achieve universal health coverage, will inform other systems in China as well as other relevant countries on their way to universal coverage. The paper first presents the development of Zhuhai's basic health insurance system chronologically; then comprehensively describes the background and the key components of the common disease outpatient benefit package; followed by a comparison with the common practices of outpatient benefit package of other areas of China and four neighboring countries. It also summarizes the strengths and weakness of the package, and lists the remaining research questions for future studies. The common disease outpatient benefit package of Zhuhai has helped to improve the universal health coverage of Zhuhai in the following aspects: securing all citizens' access to the common disease outpatient services under the basic health insurance coverage; containing the rapid growth of health expenditures; enhancing provider awareness of expenditure and encouraging cost-effective interventions through appropriate financial incentives; and shifting the focus from treatment to prevention and preventing the development of common diseases into serious conditions with high cost specialist services. The common disease outpatient benefit package greatly improved and strengthened the basic health insurance system through secured equal access to affordable outpatient care for common conditions. Limited health resources are used more efficiently by pooling the risks and by implementing capitated provider payment, which enhances the cost awareness by health care providers, to improve efficiency and creates positive incentives for health professionals for using the most cost-effective health interventions.

INTRODUCTION

In 2005, all Member States of the World Health Organization made the commitment to achieve universal health coverage. Universal health coverage cannot be achieved without evidence from research, which requires national and international support.[1] As one developing country with a large population, China's experiences in achieving universal coverage of a basic healthcare system within a short time, may contribute to the efforts of other countries with limited health resources in achieving this goal.

In 2009, China started to implement its most important health system reform of the last decade. The objective of the reform is to achieve equity and efficiency of the basic healthcare system. The principles are to strengthen primary care, and to provide universal basic health insurance coverage to its citizens through innovative mechanisms. The reform covers the following five areas: achieving equity of public health service, improving the health service delivery system (especially the three tiered rural health service delivery system and the community healthcare system), establishing universal coverage of basic health insurance, securing the supply of quality and affordable essential medicines, and reforming public hospitals.[2]

Since 2009, the national basic health insurance system has been improved greatly in the sense of increased population coverage and expansion of the benefit package. By the end of 2011, over 95% of the national population is covered by the basic health insurance programs.[3] Urban employees, urban and rural residents, and migrant workers are all included. The benefit package has also been improved continuously: the covered services have been expanded from inpatient to include outpatient care; the reimbursement rate has increased to 70%; and the maximum annual amount of reimbursement was increased to six times of the average annual salary.[4]

Zhuhai pioneered its basic health insurance system reform in advance of most other areas in China. In 2008, Zhuhai established the basic health insurance program for migrant workers. Step by step, Zhuhai also established basic health insurance programs for children and university students, and the informal employees. The city has now achieved universal coverage of the population with a basic health insurance package. The scope of the benefit package is also continuously improved. In July 2009, in the early days of the nationwide health system reform, Zhuhai created an outpatient benefit package for common disease covered by the pooled insurance fund. All the insured are allowed to enroll in this newly established package. This approach is much in advance of the rest of China, and has helped Zhuhai to achieve universal service coverage. Since then Zhuhai has further improved its

universal health coverage in three dimensions: population coverage, service coverage, and financial risk protection.

In 2011, the Zhuhai municipal Health Insurance Program established a research team to review the new common disease outpatient benefit package, and to make an assessment of its impact on utilization, costs, and quality of healthcare in Zhuhai. This is one of the articles written by the research team, which comprehensively documents the development of the new benefit package, and reports the summary results of the team's evaluation. This policy review paper describes the development of Zhuhai's common disease outpatient benefit package and the relevant supportive policies, and analyzes the significance and implications of the above policies in helping Zhuhai to further achieve universal health coverage in three dimensions.

General Information of Zhuhai

Zhuhai is located in Southern China Pearl Delta Economic Special Administration District (Guangdong province, close to Macao). The land area of Zhuhai is 1,711.2 km2. By the end of 2011, the number of residents was 1.58 million. As Zhuhai has a large number of migrant workers (47.6% of all residents), the proportion of the elderly (aged 65 and above) in Zhuhai (4.9%) is much lower than the Guangdong provincial average level (6.8% in 2011) and the national average level (8.9%). In 2011, the average life expectancy in Zhuhai was 81.4, which was seven years higher than the national average of 73.5 years. Its mean GDP per capita was over US$ 14,700 (exchange rate with CNY=6.3), which is much higher than the national average (USD 5,685, exchange rate with CNY=6.3). Its annual income per capita was CNY 28,731 (US$ 4,560 exchange rate=6.3), which was higher than the national average (CNY 21,810, US$ 3,462, exchange rate=6.3). Strong urbanization and a continuous influx of migrant workers are two major development characteristics of Zhuhaii.[5,6,7]

Basic health insurance system

Zhuhai achieved universal coverage of the population with health insurance through a step-by-step process over a period of about fifteen years (Box).

The employee program, the urban and rural residents program and the migrant worker program now constitute the three major programs of Zhuhai's basic health insurance system. The population coverage of these programs is shown in Table 1.

Box Development of universal basic health insurance system in Zhuhai (1998-2012)

- Urban employee program (1998)
- Migrant worker catastrophic disease insurance program (2001)
- Civil servant health insurance subsidy (2001)
- New rural cooperative medical scheme (NRCMS, 2003)
- Non-adult health insurance program (2006)
- Flexible employee and unemployed programs (2008)
- Resident program (integrated with NRCMS 2008)
- Common disease outpatient benefit package (2009)
- University student program (2010)
- Financial Health Aid program for the poor (2011)

Table 1 Population insured by the basic health insurance and enrolled by the common disease outpatient benefit package (2012)

Stratified level	Number of population (%)
Insured by the basic health insurance program (% of total resident population)[1]	1,500,851 (95)
By insurance program	
Urban employees (% of insured)	553,276 (36)
Urban and rural residents (% of insured)	427,575 (29)
Migrant workers (% of insured)	520,000 (35)
By age group	
< 18 years (% of insured)	226,180 (16)
18-65 years (% of insured)	1,213,420 (80)
> 65 years (% of insured)	61,251 (4)
Common disease outpatient benefit enrolled (% of insured)[1]	1,138,757 (76)
By insurance program	
Urban employees (% of enrolled)	394,380 (35)
Urban and rural residents (% of enrolled)	364,449 (32)
Migrant workers (% of enrolled)	381,081 (33)
By age group	
< 18 years (% of enrolled)	136,104 (12)
18-65 years (% of enrolled)	951,893 (84)
> 65 years (% of enrolled)	50,760 (4)
Total resident population[2]	1,582,620

Sources:

1. Zhuhai Human Resource and Social Security Bureau;
2. Zhuhai Statistics Bureau.

BACKGROUND OF THE COMMON DISEASE OUTPATIENT BENEFIT PACKAGE

Like most other areas in China before 2009, the basic health insurance system in Zhuhai covered only inpatient services, except some limited outpatient services for a number of specific high-cost diseases such as diabetes. These are diseases which can usually be clearly diagnosed, need long treatment courses, with high costs. These diseases were defined by the Zhuhai Human Resource and Social Security Bureau; their outpatient care costs were also covered by the pooled fund of the basic health insurance programs. The coverage started in 1999 with 17 disease, expanded to 25 in 2001, and finally listed 32 diseases (including tuberculosis, hypertension, diabetes, etc.) for adults, and 11 diseases (including tuberculosis, kidney diseases, and leukemia, etc.) for children in 2012.[8] For members of the urban employee scheme could pay outpatient care for other common diseases from a personal health saving account. Patients insured with the resident and migrant worker programs, had to pay out-of-pocket for general outpatient care. This arrangement prevented about half of insured patients from seeing doctors for common diseases. It also did not meet public expectations for a prevention-focused, health-secured model. It also did not use the principle of risk-pooling, as funds in the private accounts were for use by the individuals/families, and were not part of a pooled risk with other members of the programs. In conclusion, the full risk-sharing potential of an insurance system was not used and coverage was incomplete.

Following the successful achievement of near-universal population coverage of the basic health insurance programs, on 1 July 2009 the Zhuhai Human Resource and Social Security Bureau created a pooled insurance fund to cover outpatient care for common diseases. The pooled common disease outpatient fund (CD/OP) was created by the insurance pooled funds and local government subsidy, as well as by individuals contributions. With this new fund, the outpatient benefit packages of the basic health insurance were improved in two dimensions: both service coverage and financial protection coverage were increased. All members of any of Zhuhai's basic health insurance programs (employee, resident, and migrant worker) became entitled to the CD/OP benefit. Primary care facilities were identified as the gatekeepers to higher levels of health providers. The designated primary care facilities became the first contacts of the enrollees for outpatient care for common diseases; outpatient care for common diseases outside the designated primary care facilities without referrals were not covered by the pooled CD/OP fund. The coverage of the CD/OP benefit includes all diagnostic and treatment items (including medicines) that are listed by the basic health insurance programs and allowed to be delivered by the primary care facilities.[9]

By July 2012, 46 of 235 primary care facilities (including community health centers and their

Table 2 Healthcare facilities designated by the basic health insurance in Zhuhai (2012)

Type of health facilities	Number of health facilities (%)
Non-health insurance affiliated healthcare facilities	387 (61% of all healthcare facilities)
Insurance affiliated healthcare facilities	249 (39% of healthcare facilities)
Tertiary hospitals	5 (2% of health insurance affiliated healthcare facilities; 100% of tertiary hospitals; 100% public)
Secondary hospitals	9 (4% of health insurance affiliated healthcare facilities; 100% of secondary hospitals; 60% public/40% private)
Primary care facilities	235 (94% of health insurance affiliated healthcare facilities)
Health centers/stations	137 (58% of primary care facilities)
Designated for outpatient care for common diseases & specialist diseases	46 (34% of health centers/stations; 53% public/47% private)
Designated for outpatient care for specialist diseases only	91 (66 of health centers/stations; 100% private)
Clinics for outpatient care for specialist diseases only	98 (42% of primary care facilities; 16% public/14% private)
Total	636

Source: Zhuhai Human Resource and Social Security Bureau.

branches) were designated to provide outpatient services for common diseases against reimbursement by the CD/OP fund. By then, about 76% of Zhuhai's residents had registered with their preferred primary care facilities for CD/OP services. The numbers of designated facilities are presented in Table 2.

THE COMMON DISEASE OUTPATIENT BENEFIT PACKAGE AND ITS SUPPORTIVE POLICIES

The Zhuhai common disease outpatient benefit package has five stated policy objectives: a) to secure all citizens' access to the common disease outpatient services under the basic health insurance coverage; (b) to contain the rapid growth of the basic health insurance expenditures, and to reduce individual out-of-pocket expenditures for common disease outpatient services; (c) to enhance awareness of expenditure by primary care providers through financial incentives. With the incentives, providers were free to use common disease fund and encouraged to use the most cost-effective health interventions; (d) to shift focus of services from treatment to prevention, to prevent unnecessary expensive services, and to prevent the development of common diseases into serious conditions which needs high cost services; and (e) to keep the viability of primary care facilities trough designation system and capitation payment.

The average cost per patient per year for the CD/OP fund was calculated on the basis of the average annual outpatient cost per person in Zhuhai community health centers

during the 4 years of 2005 to 2008. The calculation was conducted as follows: in that period, the average utilization of community health centers in Zhuhai was 3.2 outpatient visits per insured per year, at an average cost of CNY52 (US$ 7.4, exchange rate=7). The average annual outpatient cost per insured in the community health centers in Zhuhai was then estimated at CNY 166.4 (US$ 23.8, exchange rate=7), the average cost per outpatient visit in the community health centers CNY 52 multiplied by the average annual number of 3.2 outpatient visits per insured annually). Annual outpatient cost per insured in the community health centers). To be in line with internationally accepted standards for limiting individual out-of-pocket responsibility to 30% of the total costs,[10] the reimbursement rate for outpatient care for common disease in community health centers was defined as 70%. The annual outpatient cost per person for common disease was discounted with 15% considering that the pooled procurement of services might lower the costs, and that irrational expenditure components could be reduced through a different payment method. The annual capitation cost was then set at CNY 100 (US$ 14.3, exchange rate=7) per enrollee.

In 2013, to utilize the pooled common disease fund more efficiently, the Zhuhai health insurance authority then categorized the enrollees into five groups, with the cost risks ranked from low to high. The rank of the cost risk was determined by analyzing the real expenditures of the enrollees from 2009 to 2013 as a function of their age.[11] (Table 3)

Table 3 Common disease outpatient benefit package enrollee capitation criteria in Zhuhai

Groups	Age groups (from <1 to >90)	Annual capitation criteria (CNY)
Group 1	<1, 14-25	42
Group 2	1, 10-13, 26-32, >90	78
Group 3	2, 7-9, 33-52, 88, 89	120
Group 4	6, 53-64, 81, 83-87	168
Group 5	3-5, 65-80, 82	210

Source: Zhuhai Human Resource & Social Security Bureau.

The CD/OP benefit is funded by the following components: the employee program pooled fund, the private health saving accounts of the employees, the nonemployee pooled fund, the migrant worker program pooled catastrophic fund, the resident program pooled fund, the government subsidy, and individual contributions.[9]

The coverage of the CD/OP package includes all outpatient services as defined by the basic health insurance programs. It does not cover those diseases that were already covered by the outpatient package for specialty care. There are no deductibles or

maximum reimbursement of outpatient expenditure for common disease. Referral is allowed in case of need, which is set up to relieve the tension between the increasing health needs and the service capacity of the primary care facilities. Of all expenditure incurred, the fund pays 70% and patient pays 30%. In the case of referral to a higher level of care, the patient has to pay 70% of outpatient costs and the insurance covers the remaining 30%.[9] When the patient is admitted, the usual insurance cover for inpatients takes over.

The Zhuhai Human Resource and Social Security Bureau designated primary care facilities as outpatient care providers for common diseases, eligible for reimbursement under the CD/OP fund. There were two considerations for targeting primary care facilities for the new package. First, in 2005 the cost per visit in community health facilities was only 40% of that in the public hospital.[12]

Second, this approach was in line with the World Health Organization's primary healthcare focus on affordability, easy accessibility, and suitability. The entitled beneficiaries were requested to seek outpatient care for common diseases from the annually contracted primary care facility first. All beneficiaries have to register with a single primary care facility as their first contact. Once a year they can change and register with another designated primary care facility.

Designation of primary care facility is made following the regional health plan. The principles for designation are: (i) existing designation by the basic health insurance program; (ii) qualification to provide basic medical services as defined by the Ministry of Health for primacy care facilities; (iii) working area >1000 m2; (iv) presence of at least six registered medical doctors and nine registered nurses; (v) link to at least one tertiary or secondary hospital for technical assistance and guidance; (vi) no illegal practices during the past year. Designated facilities in remote areas and on the islands are allowed to have smaller working areas and a lower number of health practitioners.[13]

A capitated provider payment system was implemented to replace the existing fee-for-service payment when the common disease outpatient benefit package was created. An amount of 4% of the pooled common disease fund was designated for risk adjustment. Facilities are paid monthly, based on the actual costs of the preceding month, up to 96% of the maximum monthly capitated amount. A year-end settlement is made to clear the annual expenditures in each July.[11]

Actual annual expenditures are settled if they are within 96% of the annual prorated payment amount. The full annual capitated amount is paid at the yearend if the actual annual

expenditures achieved 96% of annual prorated payment amount (and above). Costs that exceed the annual capitated amount are not paid.[8]

Several supportive policies were implemented to control the co-payments and the quality of care. For example, the maximum patient payment for non-reimbursed services (including non-reimbursed medicines) should be no more than 20% of the total cost of health services given to the enrolled patient within one financial year; the annual total referral outpatient expenditures shall be no more than CNY 1,500 (US$ 214, exchange rate=7, including co-payments by patients); patients' satisfaction surveys were conducted and prescriptions were audited.[8]

The Zhuhai health insurance programs conduct regular and irregular inspections of the designated primary care facilities. In addition, the insurance programs also work with the health authority to carry out year-end inspections of the designated primary care facilities. The inspection includes a review of the designation qualification, expenditures, quality of care, patient-doctor relationship, health management, etc.

The inspection results are recorded in scores in which the results of regular inspections and year-end inspections have the same weight. The score determines the level of year-end liquidation. If the score is ≥90, all expenditures are reimbursed; if the score is <90, a proportional cost is deducted from the final year payment (1‰ reduction for each point of score, up to a maximum of 4% of the prorated payment amount). If the score is ≤70 the facilities will be named and listed, and will be required to correct their performance. Facilities with insufficient correction within required time period will be disqualified for the next two years. If the score is ≤60, facilities will be directly disqualified for the next two years. For designated primary care facilities in the public sector, which implement the policy of separation of revenues and expenditures, the inspection result is linked with the payment of the government subsidy.[13]

COMPARISON OF THE OUTPATIENT BENEFIT PACKAGES IN ZHUHAI CITY WITH OTHER AREAS OF CHINA AND FOUR ASIAN COUNTRIES

We compared the outpatient benefit package of Zhuhai city with the common practices of other areas in China, as well as with the results of a cross-country health insurance scheme comparison study in Asia.[14] (Table 4)

Policy objectives

As mentioned in the section of "The Common Disease Outpatient Benefit Package and Its Supportive Policies", Zhuhai city has comprehensive policy objectives in five aspects.

However, other areas of China usually have only some of the five objectives, either focusing on universal service coverage, or focusing on cost containment.[15] Thailand intends to secure its citizens equal access to a minimum package, and the other three Asian countries expand service coverage from inpatient care to outpatient care step-by-step.

Targeted population

Zhuhai city targets all insured residents, including the employees who already have private health saving accounts to cover the outpatient care for common disease. Broader population coverage led to larger pooling of funds and risks. Common practices in other areas of China only target those who were not covered by the employee program or the new rural cooperative medical scheme.[16] The targeted population of the outpatient benefit package is heavily subsidized by the government. Thailand achieved universal population coverage. The other three Asian countries target specific populations, and are in process of achieving universal population coverage.

Targeted services

Zhuhai's outpatient benefit package covers both common disease and specialized diseases, but is now financed separately by different pooled insurance funds. Most other areas of China, like Beijing and Shanghai, operate an integrated pooled outpatient fund for both common disease and specialized disease.[14,17-19] Except Indonesia, which excludes primary care consultations, Thailand, Philippines and Vietnam all target both primary care and specialty consultations. Philippines and Vietnam only cover specific service items. Most insurance programs have separate packages for medical care and for medicines. Patients in countries with higher income only pay a fixed consultation fee which may include medicines. After reaching a maximum amount, patients pay nothing anymore. Patients in countries with lower income have decreased likelihood of being paid by insurance for medicines. Often only low-cost outpatient medicines are covered, with substantial copayments.

Financial risk protection

Zhuhai city has stronger financial protection to the outpatient benefit package enrollees than most of the other areas of China. Unlike common practices in other areas of China, Zhuhai city is one of the only two cities without deductibles and without a ceiling for reimbursement of outpatient care for common disease. Thailand charges a small fixed amount for outpatient services. The other Asian countries implement tired proportion of reimbursement, with different ceilings.

Designated providers

Like most of the other areas of China, Zhuhai city targets all types of primary care

Table 4 Outpatient benefit packages in Zhuhai, other areas of China and four Asian countries.

	Zhuhai city	Common practices in other areas of China	Thailand	Indonesia	Philippines	Vietnam
Policy objectives	Comprehensive	Either universal service coverage, or cost containment	Equal access to a minimum package	Expanded population and service coverage		
Targeted population	Universal population coverage	Who were not covered by employee program, and new rural cooperative medical scheme	Universal population coverage	Specific populations are targeted, in process of achieving universal population coverage		
Targeted services	All outpatient services as defined for the primary cares, specialized diseases are managed separately	Outpatient care for common disease and specialized disease are managed integrated	Outpatient care for both common disease and specialized disease	Primary care consultations are not covered	Only specific medicines are covered	
Financial protection	No deductibles & ceiling on reimbursed outpatient expenditure, 70% insurance copayment	Deductible & ceiling on reimbursement, average 50% co-payment, lower individual co-payment for primary care	Fixed fee	Different categories of ceiling with tired fix proportion of reimbursement		
Designated providers	Public and private primary care, absence of compulsory referral policy	All levels of public providers, no compulsory referral policy	All levels of public and private care			
Provider payment	Capitated plus performance based payment method	Fee for service and global budget	Capitation and fee for service for different programs	Shift from retrospective to prospective payment	Fee for service subject to a ceiling per cost item	Fee for service

facilities (public and private) for the delivery of outpatient services. In most other areas of China, only public facilities can be usually designated and private ones are excluded. However, in Zhuhai the percentage of private facilities is much higher than in the rest of China, and 52% of the CD/OP benefit package designated primary care facilities are privately run. This unique situation has enabled competition between public and private primary care, which is in line with the trend of the national health system reform toward public–private partnerships. Other Asian countries usually contract a preferred network of both private and public providers as well.

Provider payment

Zhuhai city implements a capitated provider payment method, plus an additional pay for good performance. Such payment method raises cost awareness by health care providers and leaves them some autonomy. Risks are adjusted through the tiered capitation levels for different age groups. Quality of care is secured through pay-for-performance assessment. Most of the other areas of China still keep the traditional fee-for-service payment, sometimes combined with a global budget payment.[17,20-22] Thailand uses a capitated payment for its Universal Coverage Program and fee-for-service for its Social Health Insurance Program. Indonesia is in the process of shifting from retrospective to prospective payment. Philippine implements a fee-for-service payment method with a ceiling per cost item. Vet Nam still uses the traditional fee-for-service payment.

DISCUSSION

The introduction of the Zhuhai common disease package has many positive effects. First of all, the new package corrects the negative effects of the previous system whereby half of insured patients paid for outpatient care through their private health saving accounts, and the other half were not insured for outpatient care and paid out-of-pocket. The new package secures access to affordable outpatient care for common disease of the elderly, the sick and the other vulnerable groups who did not have private health saving accounts, or whose accounts were not enough to cover their outpatient expenditure for common disease. The improved benefit package therefore has the potential to greatly improve and strengthens the basic health insurance system. Second, the system become less vulnerable and more efficient in using health resources by pooling the risks across all insured, including the employees who have private health savings account. Third, the focus on prevention and treatment at primary care facilities is in line with the key principles of the current national health system reform: strengthening primary care and securing sufficient financing for basic care needs. Fourth, removing deductibles and a maximum level of reimbursement effectively protects patients against excessive out-of-pocket payments and greatly relieved the financial burden of the enrollee. And finally, the capitated provider payment has the potential to

enhance the cost awareness of providers while still allowing them to manage their own funds. This is again consistent with the goal of national health system reform to improve efficiency and create positive incentives for health professionals.

There are also a few negative points to the new benefit package. First, there is no compulsory referral mechanism in place and the utilization of outpatient care therefore may need to be further promoted, in order to change the preference of the general public in seeking expensive hospital care for common diseases. Second, the introduction of the outpatient benefit package includes a set of policies to encourage cost-effective treatment, such as capitated provider payment and a financial reward for those who delivered the required quantity of services. Although cost containment awareness by providers is potentially raised, perverse incentives still need to be removed, and new policies are needed to promote cost-effective prescribing behavior rather than cost containment only.

More research is needed to measure the exact effect of the new package, to optimize the current payment and reward policies and to remove negative incentives. The experiences with the Zhuhai common disease outpatient benefit package can then form a basis for innovative management strategies for high cost diseases.[23] As expensive outpatient and inpatient care are critical for in-depth public hospital reforms in China in the next steps, further projects are needed to transform the lessons and experiences of the Zhuhai common disease outpatient benefit package into operational strategies for the specialty care benefit package.

CONCLUSION

The common disease outpatient benefit package of the basic health insurance program in Zhuhai secures equal access to affordable outpatient care for common disease, which effectively protects patients against excessive out-of-pocket payments and greatly relieves the financial burden of the enrollee, especially the vulnerable population. The improved benefit therefore greatly improves and strengthens the basic health insurance system. Limited health resources are used more efficiently by pooling the risks and implementing capitated provider payment, which enhances the cost awareness of providers and expected to improve efficiency and create positive incentives for health professionals in using the most cost-effective health interventions. In summary, it helps to achieve universal health coverage in Zhuhai city.

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Chapter 5

The Effects of Comprehensive and Integrated Health System Reform Policies on Medicines

5.2 Impacts on Utilization, Costs, and Quality of Care of a New Insurance Benefit for Treating Common Primary Care Conditions in Zhuhai, China

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ABSTRACT

In 2009, China started to implement its most important health reform of the last decade. Many local innovative reforms have been implemented. Few were comprehensively assessed with appropriate method. In this paper, complementary sources of routinely collected data were systematically collected and analysed to assess the impact of a local health insurance reform. We used longitudinal health insurance claims data, health administrative data and primary care facility data to assess trajectories in outpatient visits, inpatient admissions, cost per common disease outpatient (CD/OP) visit, and prescribing indicators over time. We conducted segmented regression analyses of interrupted time series data to measure changes in level and trend overtime, and cross-sectional comparisons against external standards after the introduction of a new primary care insurance benefit with capitated provider payment. The number of total outpatient visit at 46 primary care facilities (designated by the CD/OP benefit as of July 2012) increased 46,895 visits/month (p=0.004, 95% CI: 15,795~77,994); the average number of CD/OP visits reached 1.84/year/enrollee in 2012; monthly inpatient admissions dropped from 6.4 (2009) to 4.3 (2012) per 1,000 enrollee; the average total cost per CD/OP visit dropped CNY 15.40 (p=0.16, 95% CI: -36.95~6.15); injectable use dropped 7.38% (p=0.03, 95% CI: -14.08%~-0.68%); antibiotic use was not improved. Zhuhai's new CD/OP benefit with capitated provider payment has expanded access to primary care, which may have led to a reduction in expensive specialist inpatient services for CD/OP benefit enrollees. Cost awareness was likely raised, and rapidly growing expenditures were contained. Although having been partially improved, inappropriate prescribing of antibiotics and injectables was still prevalent. More explicit incentives and specific quality of care targets are needed to be incorporated into the pay-for-performance system of capitated provider payment, in order to promote scientifically sound and cost-effective care and treatment.

INTRODUCTION

China's health system reform seeks to strengthen the universal basic health insurance coverage and primary care.[1] Local innovations are essential for achieving universal health coverage. An important example is the introduction of health insurance for common diseases treated in primary care settings in Zhuhai, a municipality of 1.58 million[2] in Guangdong province in Southern China, characterized by urbanization and an influx of migrant workers.

Prior to 2009, health insurance focused on inpatient (IP) services, and outpatient (OP) care for a limited number of chronic conditions only.[3] Health insurance did not cover OP care for

common primary care diseases (CDs) such as diabetes and hypertension at an early stage, except for urban employees with medical savings accounts (MSAs) for this purpose. Such accounts, being personal and private, do not share risks between insurance members, and have an adverse effect on insurance risk pooling.[4,5] Undesirable side effects such as reduction in equity may be introduced into the system.[6] The lack of primary care OP coverage of insurance schemes was generally seen as inefficient and inequitable,[7,8] as such arrangements may create barriers to accessing services among the poor and other under privileged groups.[9]

In 2009, the Zhuhai Municipal Health Insurance (ZMHI) started to integrate insurance benefits across three insurance programs: urban employees, urban and rural residents, and migrant workers. In July 2009, responding to provincial and central government policy guidance, the ZMHI created the so-called "common primary care disease outpatient benefit" (CD/OP).[10] Compositions of the pooled CD/OP fund are listed in Table 1. All members of any of the three insurance programs could voluntarily enroll in the CD/OP benefit, and register themselves with one preferred designated primary care facility. The designation criteria included: regional health planning; insurance affiliation; primary care provider qualification; required working area and professional staff, etc.[11] The CD/OP benefit covers all diagnostics and treatments (including medicines) as listed by the insurance programs for primary care services, except those already covered by the package for specialized OP care (a limited number of diseases defined by the insurance programs, which can be diagnosed with clear criteria, and need long term treatment courses with high costs). Firstly in 1999 with 17 diseases, expanded to 25 in 2001, and finally listed 32 for adults and 11 for children in 2012).[3] With the introduction of the CD/OP benefit, an annual capitated provider payment replaced the fee-for-service system. Of the total CD/OP benefit costs, the insurance pays 70% and patients 30%. No reimbursement maximums are set, and referral is allowed when needed. CD/OP care outside the designated facilities is not covered by the pooled CD/OP fund, but can be paid by MSAs. Being referred to a higher level of care, patients pay 70% of OP costs and the insurance covers the rest. When a patient directly presents to a hospital for specialist conditions or is admitted, the existing coverage for specialized OP care or IP coverage applies. No cost overruns are paid to the provider if actual expenditures are higher than the annual capitated amounts. A pay-for-performance system was implemented together with the capitated provider payment. These included regular and irregular inspections and year-end inspections. The inspections review the qualification, general management, policy understanding, compliance of prescription and pricing regulation, expenditures, patients' satisfaction, management of chronic conditions, etc. of the designated facilities. The inspection results were recorded in scores, which determined the level of year-end settlement.[11]

Table 1 Composition of the contributions to the pooled common disease outpatient fund per insured per year (CNY)

	Per urban employee	Per urban and rural resident	Per migrant worker
Pooled insurance funds	50	50	100
Medical savings accounts	50	NA	NA
Government subsidies	0	25	0
Individual contributions	0	25	0
Total	100	100	100

Source: Zhuhai Human Resource and Social Security Bureau.

In 2011, the central government called for full coverage of OP care for all urban residents across the country. By July 2012, the basic health insurance system of Zhuhai covered 95% of its resident population, including formal and informal employees, retired employees, unemployed, children, university students, and migrant workers. 79% of the insured and 73% of the resident population had registered with their preferred primary care facilities for CD/OP services (Table 2). That same year, the ZMHI established a research team to assess impacts of the CD/OP benefit with capitated provider payment on utilization, costs, and quality of care. The hypotheses were that the introduction of the CD/OP benefit with capitated provider payment would lead to increased access to primary care and fewer admissions; that OP expenditures would be contained; and that over prescribing of antibiotics and injectables would decrease. This paper reports the results of evaluation.

METHODS

Study design

We conducted a longitudinal study of health care utilization, expenditures, and quality of care in Zhuhai between August 1, 2008 and July 31, 2012. We used three complementary sources of data to assess trajectories in key outcome measures over time, and a fourth data source to generate indicators for cross-sectional comparison against external standards (Zhuhai targets, national and international levels).

Population and settings

The study population consists of 1.44 million CD/OP enrollees in three major insurance programs (urban employees, urban and rural residents, and migrant workers) between1 August 2008 and 31 July 2012. The total resident population and the insured population were used for comparison. In July 2009, the ZMHI designated 27 health centers and their branches as CD/OP designated facilities; another 15 were designated in 2010 and four in 2011. By July 2012, of the 235 insurance-affiliated primary care facilities, 46 were designated to provide

Table 2 Population and facility characteristics, August 2008-July 2012

Population characteristics	2008	2009	2010	2011	2012
Resident population, n[1]	1,511,150	1,541,762	1,561,569	1,567,646	1,582,620
Insured population, n (%)[2]	1,204,978 (80)	1,261,734 (82)	1,369,867 (88)	1,440,717 (92)	1,500,851 (95)
By insurance program					
Urban employees, n (% insured)	499,620 (42)	434,203 (36)	506,778 (38)	510,380 (36)	553,276 (36)
Urban and rural residents, n (% insured)	375,416 (31)	414,943 (31)	413,438 (29)	424,337 (29)	427,575 (29)
Migrant workers, n (% insured)	329,942 (27)	412,588 (33)	449,651 (33)	506,000 (35)	520,000 (35)
By age group					
< 18 years, n (% insured)	208,803 (17)	225,301 (17)	223,875 (16)	225,164 (16)	226,180 (16)
18-65 years, n (% insured)	948,388 (78)	1,056,712 (79)	1,143,902 (80)	1,158,099 (80)	1,213,420 (80)
> 65 years, n (% insured)	56,499 (5)	53,055 (4)	55,491 (4)	58,182 (4)	61,251 (4)
CD/OP enrollees, n (% insured)[2]	n/a	651,555 (52)	883,062 (64)	1,074,800 (74)	1,138,757 (76)
By insurance program					
Urban employees, n (% CD/OP enrollees/% insured)	n/a	251,259 (39/58)	323,573 (37/64)	372,366 (35/73)	394,380 (35/71)
Urban and rural residents, n (% CD/OP enrollees/% insured)	n/a	217,107 (33/52)	290,155 (33/70)	354,233 (33/83)	364,449 (32/85)
Migrant workers, n (% CD/OP enrollees/% insured)	n/a	183,496 (28/45)	270,141 (30/60)	349,357 (32/69)	381,081 (33/73)
By age group					
< 18 years, n (% CD/OP enrollees)	n/a	97,018 (15)	125,533 (14)	133,183 (12)	136,104 (12)
18-65 years, n (% CD/OP enrollees)	n/a	519,600 (80)	714,853 (81)	893,277 (83)	951,893 (84)
> 65 years, n (% CD/OP enrollees)	n/a	34,937 (5)	42,676 (5)	48,340 (5)	50,760 (4)
Facility characteristics[2]					
All health care facilities, n	649	668	685	637	636
Insurance affiliated facilities, n (% of all)	221 (34)	238 (36)	239 (35)	238 (37)	249 (39)
Primary care, n (% of insurance affiliated)	207 (94)	226 (95)	226 (95)	225 (95)	235 (94)
Health centers/stations, n	109	126	127	126	137
CD/OP designation, n (% of health centers)	n/a	27 (21)	42 (33)	46 (37)	46 (34)
Not-CD/OP designation, n (% of health centers)	109 (100)	99 (79)	85 (67)	80 (63)	91 (66)
Clinics, n	98	100	99	99	98
Secondary care, n	9	7	8	8	9
Tertiary care, n	5	5	5	5	5
Not-affiliated facilities, n (% of all facilities)	428 (66)	430 (64)	446 (65)	399 (63)	387 (61)

Sources:
1. Zhuhai Statistics Bureau;
2. Zhuhai Human Resource and Social Security Bureau.

Abbreviation:
CD/OP means common disease outpatient.

care covered by the CD/OP benefit. Zhuhai also has nine secondary and five tertiary hospitals affiliated with the insurance program for covered IP care. All insurance-affiliated health facilities provide covered specialist OP care (Table 2).

Data sources

Insurance claims data for CD/OP care were only available with the implementation of the CD/OP benefit, starting in August 2009. From August 2009 onwards, insurance claims data were used to assess financing of OP visits, and to display trajectory of CD/ OP utilization and disaggregated for different insurance and age groups. Insurance claims data for IP care were used to construct the indicator of IP utilization. Insurance enrollment data provided the denominators for the time period of August 2008 (one year before CD/OP benefit introduction) to July 2012 (one year after the latest facility designation).

Insurance claims data were supplemented with monthly administrative data from the Zhuhai Municipal Health Bureau. Aggregated monthly administrative data were available for all health facilities (n=636 in 2012), and for the subset of primary care facilities designated for the CD/OP benefit (n=46 in 2012). The health administrative data included information on health service utilization for both OP and IP care. We used OP utilization data from the 46 primary care facilities (designated by the CD/OP benefit as of July 2012) to construct time series of all kinds of OP visits indicator August 2008-July 2012.

The studied primary care facilities were selected from the first group of CD/OP benefit designated facilities (n=27, designated in July 2009) with a condition of having electronic records before July 2009 (n=4). These facility electronic records could separate the information on specialized OP care from the CD/OP care. We collected prescription and expenditure data for CD/OP care before August 2009 from the facility electronic records (August 2008-July 2009). We combined this with the insurance claims data (August 2009-July 2012) to construct the time series of total cost per CD/OP visit and prescribing quality indicators August 2008-July 2012.

For the comparisons of IP utilization indicator among different populations in Zhuhai, data for all resident population in all health facilities were collected from the health administrative system; data for all insured and CD/OP benefit enrolled were extracted from the insurance claims data. For the comparisons of OP utilization, quality of care indicators with external standards, we sourced public available local targets, average national and international levels.

Outcome measures

Service utilization indicators are: (a) the monthly number of total OP visits at 46 primary care

facilities (designated by the CD/OP benefit as of July 2012) (health administrative data August 2008-July 2012), and that of OP visits paid by the pooled CD/OP fund (insurance claims data August 2009-July 2012); (b) the annual number of CD/OP visits per enrolled; and (c) the monthly numbers of hospital discharges per CD/OP enrolled, per insured (insurance claims data 2009-2012), and per resident population (health administrative data 2009-2012). The numbers of resident population were from the Zhuhai Statistics Bureau, and the insurance membership data came from Zhuhai Insurance Bureau. Health service expenditure indicators are: (d) the total cost per CD/OP visit (facility electronic records of the studied CD/OP designated primary care facilities August 2008-July 2009, and insurance claims data August 2009-July 2012). Quality of care indicators focus on prescribing behavior: (e) the proportions of CD/OP visits during which at least one antibiotic and injectable was prescribed (facility electronic records of the studied CD/OP designated primary care facilities August 2008-July 2009, and insurance claims data August 2009-July 2012).

Statistical analysis

We illustrate trajectories of indicators based on longitudinal data before and after the implementation of the CD/OP benefit: the number of total OP visits at 46 primary care facilities (designated by the CD/OP benefit as of July 2012); and the total cost per CD/OP visit, the proportions of CD/OP visits with at least one antibiotic and injectable prescribed in the studied primary care facilities (designated in July 2008). Graphs show the monthly outcomes of these indicators August 2008-July 2012. We analyze longitudinal time series data using segmented linear regression models and available statistical software (which controls for secular trends and also adjusts for potential serial correlation of the data).[12,13] Segmented linear regression divides the time series into pre- and post- CD/OP introduction segments, and we compared the change in trends before and after implementation of the CD/OP benefit with capitated provider payment. STATA12.0 was used to perform regression analyses. As the CD/OP benefit was announced in July 2009, we regarded August 2009 as the intervention time point for the regression analysis to leave one month transition for the introduction of the new benefit with capitated provider payment. For indicators for which we only had data starting with the implementation of the CD/OP benefit in 2009 (the number of CD/OP visits per enrolled and by subgroups; the proportion of the number of CD/OP visits to total number of OP visits covered by insurance; the hospital discharge rates of CD/OP enrollees), we either present the annual values or display indicator trends following the introduction of the CD/OP benefit in 2009.

RESULTS

Population and facilities

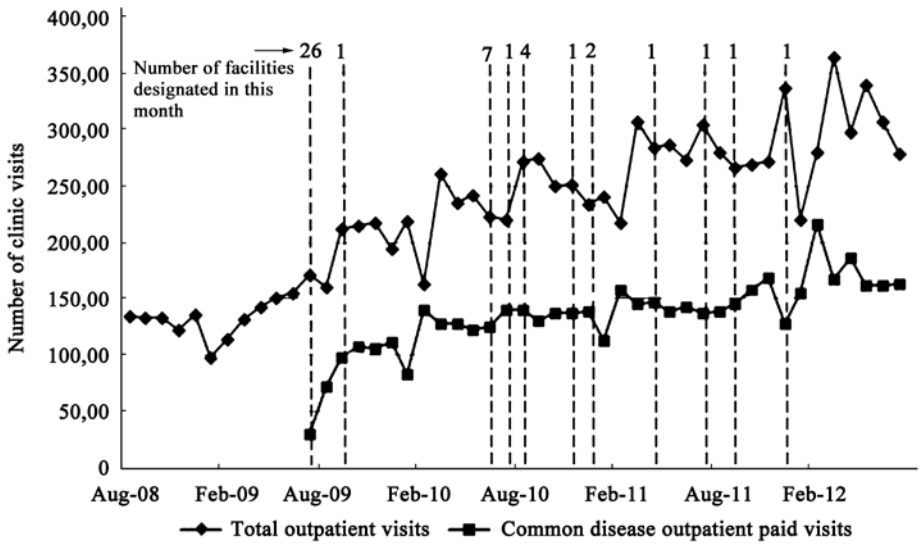
Table 2 shows the population distribution in each of the five study years. During 2009-

2012, the population of Zhuhai increased from 1,511,150 to 1,582,620 (increased 4.7%), with the proportion of insured population increasing from 82% to 95%; enrollment in the CD/OP benefit increased to 76% of the insured population (71%, 85% and 73% for the insured urban employees, urban and rural residents and migrant workers, respectively); participation in the new package by the three insurance groups had become equal (32%-35%) with 84% of CD/OP enrollees between 18 and 65 years old. Table 2 also shows the numbers, types, and insurance affiliations of health care facilities in Zhuhai. By 2012, 46 of the 137 insurance-affiliated health centers were designated as CD/OP providing facilities.

Utilization

The monthly number of all kinds of OP visits at 46 primary care facilities (designated by the CD/OP benefit as of July 2012) and that of OP visits covered by the pooled CD/OP fund during August 2008-July 2012 are presented in Fig. 1. The regression results (Table 3) showed that, prior to the introduction of the CD/OP benefit with capitated provider payment, the number of all kinds of OP visits steadily increased (p=0.19). In August 2009, it suddenly increased 46,895 visits/month (p=0.004, 95% CI: 15,795~77,994). In the following three years, it continued to increase with faster growth rate (p=0.74). The proportion of the number of OP visits paid by the pooled CD/OP fund to the number of all kinds of insurance covered OP visits rose from 6.7% in 2009 to 24.3% in 2012 (Table 4).

Fig. 1 Monthly number of total outpatient visits at 46 primary care facilities (designated by the common disease outpatient benefit as of July 2012) and outpatient visits paid by the pooled common disease outpatient fund August 2008-July 2012



Sources: Health Bureau (total outpatient visits) and health insurance (outpatient visits paid by the pooled common disease outpatient fund).

Table 3 Estimated level and trend changes of service utilization, cost and quality of care indicators following the implementation of the CD/OP benefit in the designated primary care facilities

		Baseline trend	Level change	Trend change
Outcome	Intercept	(P value, 95% CI)	(P value, 95% CI)	(P value, 95% CI)
Number of all kinds of outpatient visits [1]	117,606	2,666 (0.19, -1,401~6,734)	46,895 (0.004, 15,795~77,994)	673 (0.74, -3,453~4,799)
Total cost per CD/OP visit [2]	75.74	1.32 (0.24, -0.90~3.55)	-15.40 (0.16, -36.95~6.15)	- 0.81 (0.48, -3.10~1.47)
% CD/OP visits with at least one antibiotic [2]	66.68	**-1.37 (0.02, -2.54~-0.20)**	-1.11 (0.76, -8.34~6.11)	**1.52 (0.02, 0.21~2.83)**
% CD/OP visits with at least one injectable [2]	38.73	0.68 (0.14, -0.24~1.59)	**-7.38 (0.03, -14.08~-0.68)**	-0.92 (0.06, -1.89~0.05)
% CD/OP visits for ARI with at least one antibiotic [2]	86.20	0.16 (0.63, -0.49~ 0.81)	**-7.37 (0.002, -11.95~-2.79)**	-0.57 (0.11, -1.27~0.13)
% CD/OP visits for ARI with at least one injectable [2]	74.99	-0.68 (0.34, -21.08~0.74)	**-16.52 (0.004, -27.39~-5.65)**	0.39 (0.59, -1.07~1.85)

Sources:

1. Health administrative data (August 2008-July 2012) of 46 primary care facilities (designated by the CD/OP benefit as of July 2012);
2. Electronic data (August 2009-July 2012) from the sample primary care facilities (designated by the CD/OP benefit in July 2009).

Abbreviations:

CD/OP means common disease outpatient; ARI means acute respiratory infection.

Note:

Bold signifies statistically significant (p<0.05).

Table 4 Financing of insurance covered OP visits in Zhuhai, 2009-2012

Year	Insurance-covered OP visits	Paid by the medical savings accounts		Paid by the specialist disease OP fund		Paid by the pooled CD/OP fund	
	n	n	%	n	%	n	%
2009	7,070,319	6,193,650	87.60	403,961	5.71	472,708	6.69
2010	8,638,712	6,340,020	73.39	563,317	6.52	1,735,375	20.09
2011	8,947,839	6,437,359	71.94	537,171	6.00	1,973,309	22.05
2012	8,849,100	6,132,698	69.30	565,748	6.39	2,150,654	24.30

Source:
Zhuhai Human Resource and Social Security Bureau.
Abbreviations:
OP means outpatient; CD/OP means common disease outpatient.

The annual utilization rates for various insurance programs, age groups, and some diseases are presented in Table 5. In 2012, the average number of OP visits covered by the pooled CD/OP fund

Table 5 Annual numbers of common disease outpatient visits per common disease outpatient benefit enrollee, August 2009-July 2012

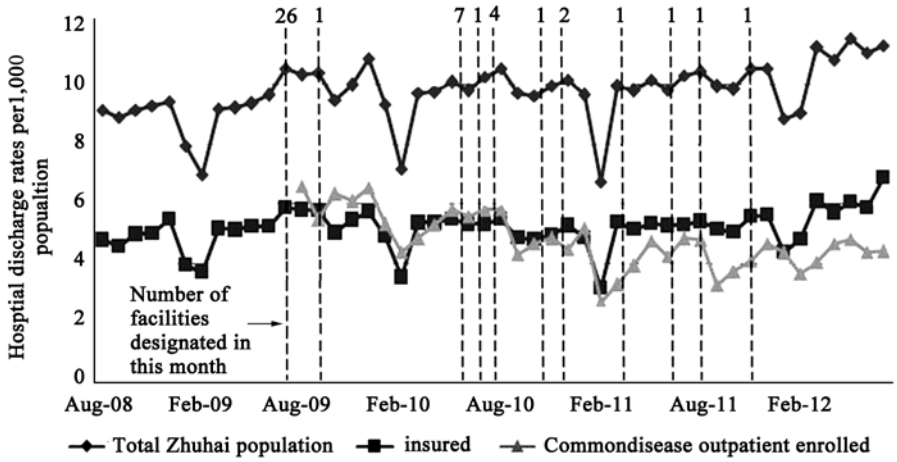
Stratified group		Enrollee category		Annual OP visits for CD per CD/OP enrollee			
				2009	2010	2011	2012
Whole population				1.97	1.87	1.88	1.84
By age group		<18		3.11	2.78	3.48	3.11
		18-65		1.61	1.58	1.53	1.53
		>65		4.06	4.10	3.99	4.01
By insurance program		Urban & rural residents		1.99	2.06	2.10	2.08
		Urban employees		2.78	2.47	2.53	2.44
		Migrant workers		0.97	1.00	0.98	0.97
By disease group	Enrollees with diabetes	All enrolled patients with diabetes		16.72	14.67	15.64	14.99
		By age group	<18	12.00	n/a	12.00	n/a
			18-65	16.39	14.52	15.68	14.95
			>65	18.12	15.32	14.56	15.13
		By insurance program	Urban & rural residents	16.36	14.52	15.02	14.66
			Urban employees	17.88	15.00	16.45	15.82
			Migrant workers	12.80	14.55	17.26	14.66
	Enrollees with hypertension	All enrolled patients with hypertension		18.12	17.93	18.24	18.06
		By age group	<18	12.00	12.00	12.00	12.00
			18-65	17.64	17.85	18.00	17.83
			>65	17.81	18.13	18.84	18.80
		By insurance program	Urban & rural residents	17.93	17.70	18.08	17.84
			Urban employees	17.55	18.44	18.85	18.65
			Migrant workers	16.16	17.18	16.15	16.57

Source:
Zhuhai Human Resource and Social Security Bureau.
Abbreviations:
OP means outpatient; CD means common disease; CD/OP common disease outpatient.

was 1.84/enrollee/year. Among the enrollees, urban employees had a higher use (2.44/year) and migrant workers was lower (0.97/year); members above 65 years of age had a higher use (4.01/year) and members between 18 to 65 years age was lower (1.53/year). The numbers of visits for diabetes and hypertension patients for all age groups (except <18) and insurance programs were at the same level, at an average level of 14.99 and 18.06/patient/year respectively.

The monthly hospital discharge rates for CD/OP benefit enrollees are presented in Fig. 2. The hospitalizations steadily decreased from a monthly average of 6.4/1,000 enrollees in August 2009 to 4.3/1,000 enrollees in July 2012. In comparison, in 2012, the average monthly hospital discharge rates were 5.7/1,000 people for all insured, and 10.0/1,000 people for all the resident population. Annual dips in February reflect fewer hospitalizations around Chinese New Year.

Fig. 2 Monthly hospital discharge rates of the overall resident population, the insured members, and the common disease outpatient beneficiaries, August 2008-July 2012 (per 1,000 population)



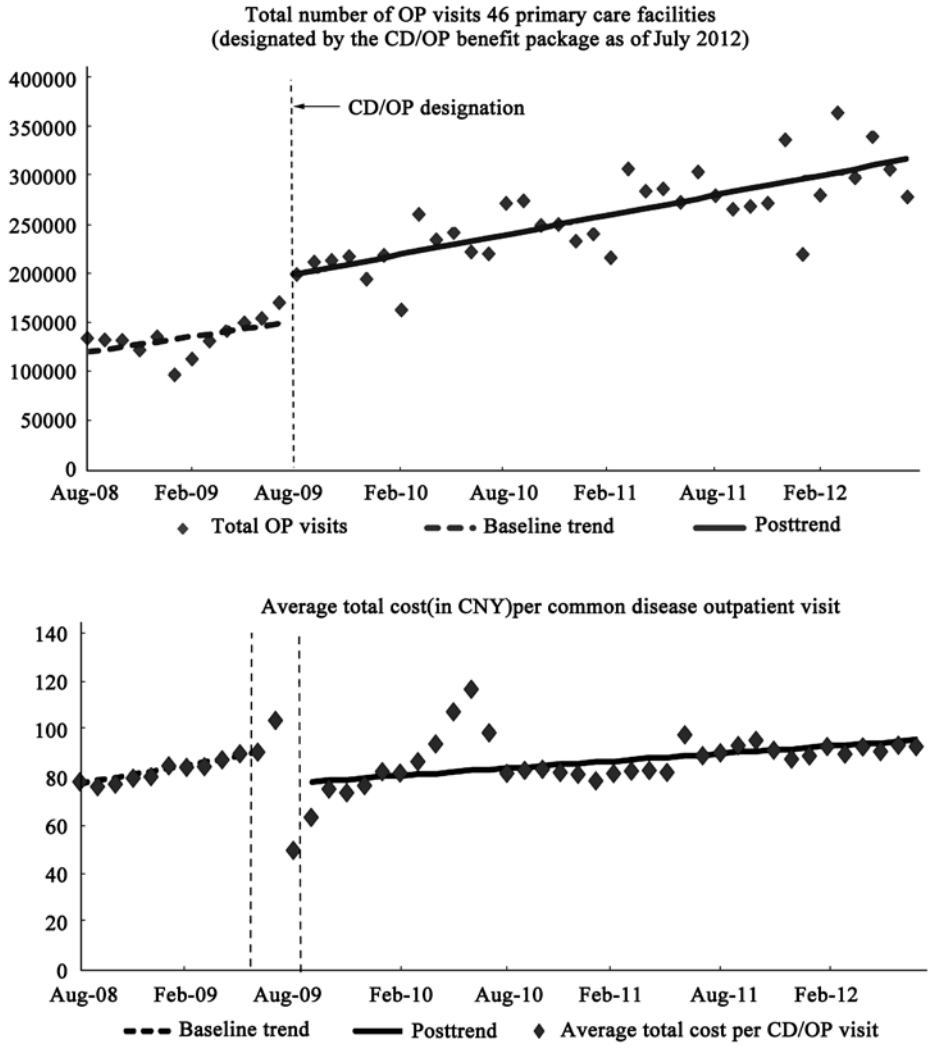
Sources: Insurance claims system (insured members and common disease outpatient enrolled populations); health bureau (overall resident population).

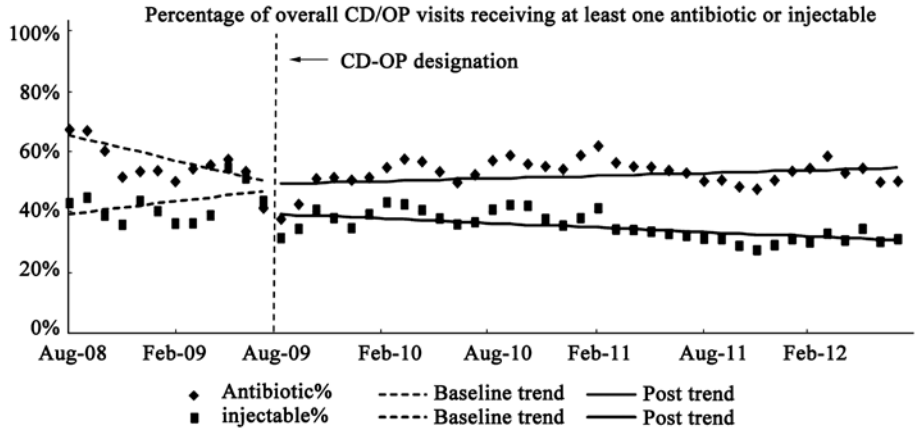
Expenditures

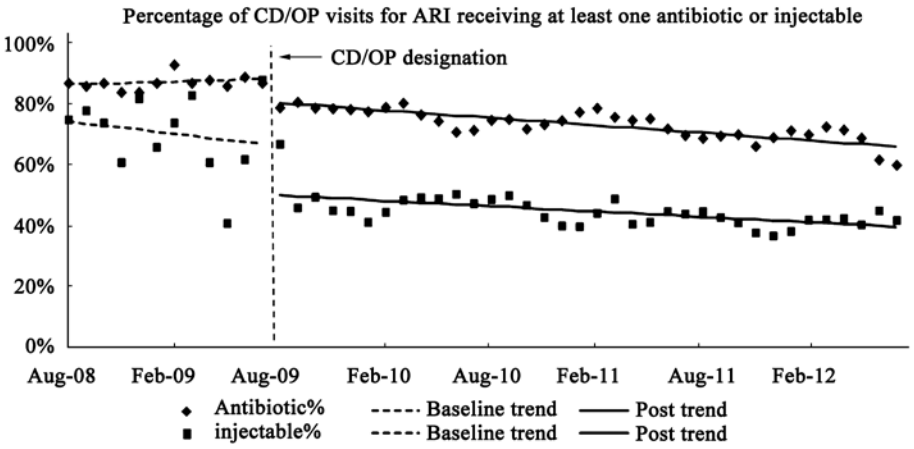
Cost data show two outlying values just before and after the introduction of the CD/OP benefit with capitated provider payment (Fig. 3). These unusual values may represent anticipatory demand by the newly designated primary care facilities intending to receive a higher capitation rate, and lower charges directly after designation due to concerns about staying within the capitated rate. We did not include these two data points in the regression analyses to avoid over estimation.

Before the introduction of the CD/OP benefit with capitated provider payment, theaverage total cost per CD/OP visit steadily increased (p=0.24). There was a sudden decrease between June and September 2009, when cost dropped CNY 15.40 (p=0.16, 95% CI: -36.95 ~ 6.15). It continued to increase slightly but at a lower rate afterwards (p=0.48) (Table 3). Peaks are visible in June 2010 and June 2011 (Fig. 3).

Fig. 3 Service utilization indicator in 46 primary care facilities (designated by the CD/OP benefit as of July 2012), cost and quality of care indicators in sample primary care facilities (designated to implement the CD/OP benefit in July 2009), August 2008 –July 2012







Source:
Studied primary care facilities designated by the CD/OP benefit in August July 2009.
Abbreviations:
CD/OP means common disease outpatient; ARI means acute respiratory infection.
Notes:
1. Vertical lines in the first, third and fourth graphs indicate the introduction of the CD/OP benefit with capitated provider payment;
2. Vertical lines in the second graph indicate a transition period around the time of the introduction.

Quality of Care

Prior the introduction of the CD/OP benefit with capitated provider payment, the proportion of number of CD/OP visits with at least one antibiotic prescribed significantly decreased (p=0.02). In August 2009, it slightly dropped (p=0.76) and reversed into a significant increasing trend afterwards (p=0.02). The proportion of CD/OP visits with at least one injectable prescribed underwent from a steadily increase (p=0.14) to a sudden drop of 7.38% (p=0.03, 95% CI: -14.08%~-0.68%) in August 2009, followed by a downward trend (p=0.06). CD/

OP treatment for acute respiratory infection (ARI) showed a steady rising of antibiotic use (p=0.63) first, significantly dropped 7.37% (p=0.002, 95% CI: -11.95%~-2.79%) in August 2009, and steadily decreased (p=0.11) afterwards. Injectables experienced from a steady decrease (p=0.34) to a sudden decrease of 16.52% (p=0.004, 95% CI: -27.39%~-5.65%) in August 2009, followed by a continued steady decrease with slower rate afterwards (p=0.59). In 2012, the proportions of CD/OP visits prescribed with at least one antibiotic and injectable were 53% and 31% (68% and 42% for ARI visits) (Table 3 and Fig. 3).

DISCUSSION

Utilization of OP care

When designing the CD/OP benefit, Zhuhai upheld the principle of providing vulnerable populations with increased access to health care services, and designing a minimum benefit package including coverage of primary care.[14] The introduction of the CD/OP benefit with capitated provider payment increased the access to primary care. Urban and rural residents and migrant workers previously did not have MSAs, were not covered by insurance for CD/OP services. They are the most vulnerable populations in Zhuhai, and benefited from the CD/OP benefit the most. Urban employees and members older than 65 years old had the highest uptake of the new package. For the treatment of diabetes and hypertension, members in different insurance groups showed a same utilization level. Although the enrolled population evenly distributed over three insurance groups, and the majorities were members aged 18-65 years, there might be a potential risk that more unhealthy population enrolled to the CD/OP benefit.[15]

However, the full impact on service utilization is not yet known, as by the end of the study period, only 34% of health centers and their branches were designated (Table 2), and only 24.3% of the numbers of insurance-covered OP visits were paid by the pooled CD/OP fund (Table 4). Unlike the countries with high performance health care systems where primary care either plays a gate keeping role to hospital care, or strong incentives for coordinated care across all levels of providers exist, and most patients enter the health system via the primary care,[16-19] there is not yet a compulsory primary care gatekeeper system in Zhuhai. The primary care has no effective financial leverage over hospital care. Although there are several incentives for the use of the CD/OP benefit: 1) contributions to the pooled CD/OP fund are automatically deducted from individual MSAs of urban employees, even if they do not enroll or not use the CD/OP care; 2) individual contribution is bundled with the premium charge of the urban and rural resident program beneficiaries; 3) no deductable for CD/OP care vs. higher deductibles for higher levels of hospital inpatient care. However, these are not enough to incentivize the use of CD/OP care, as the designated facilities yet satisfy the needs, and patients do not trust the quality of care in these facilities. Some citizens still

prefer to present themselves directly for expensive hospital care, especially urban employees who have MSAs.[15,20]

In addition, referred patients have a co-payment of 70%. This policy originally intends to prevent inappropriate referral. However, it might dis-incentivize the use of CD/OP care without a compulsory referral system for hospital care and coordination among all the existing insurance benefits (CD/OP in hospitals paid by MSAs, specialist OP and IP benefit). Patients might bypass the primary care to avoid high co-payment in case of referral, as the specialist OP and IP benefits apply more generous benefits.

Generally, primary care in China is weak, patients do not trust the quality of primary care facilities, and there is not yet sufficient coordination among different tiers of health care. All these factors make it difficult for primary care to have a gate keeping role, the core functions of primary care are not being met.[21-23] Stronger incentives for using the primary care or even a compulsory referral system for the hospital specialist care, and better coordination among insurance benefit packages of different tiers of care, are needed.

Utilization of IP care

Preventing unnecessary hospitalizations through high quality and accessible primary care is one indicator of a well performing primary care system. In Zhuhai, the monthly hospital discharge rate of the CD/OP enrolled continuously decreased during 2008-2012 (Fig. 2). This decreasing trend is contrary to the upward national trend from 7.2/1,000 population in 2008 to 9.5/1,000 population in 2011 and to 11/ 1,000 population in 2012.[24] Also, during 2011-2012, CD/OP enrollees showed lower rates of hospital discharges than all resident population and all insured population (Fig. 2), possibly indicating containment of IP care for the CD/OP benefit enrollees. It seems that the objective of keeping diagnosis and treatment of CDs at the primary care level and reducing need for expensive specialist care were achieved. This is consistent with the findings of one recent systematic review.[25] In which most studies confirmed lower hospitalization rates for ambulatory care sensitive conditions (ACSCs) with greater access to primary care.

Expenditure of OP care

Provider payment reforms have been mostly effective in influencing health expenditure patterns. Designing payment systems for primary care has increasingly looking to capitation payment in many countries.[26] In Zhuhai, when the CD/OP benefit with capitated provider payment was introduced, the average total cost per CD/OP visit dropped, although not significantly, the increasing rate of the expenditures turned to slower afterwards. This implied that the CD/OP benefit did raise cost awareness, and some expenses were probably reduced in the first months of the financial year to save the annual capitation fund. This

result is in line with the findings of many other studies in both rural and urban areas of China that, primary care provider payment reforms show effects of cost reduction.[27-30] Studies in OECD countries demonstrated similar effects.[31] The introduction of capitated physician payment in UK also succeed in containing overall cost with no evidence of cost shifting to higher level of care.[32] Social health insurance schemes in other developing countries like Argentina, Brazil, Nicaragua and Thailand also adopted capitated provider payment reforms to avoid the cost inflation experienced with fee-for-service payment.[33-35]

However, in June 2010 and 2011, the last settlement month of the financial year, there were annual cost peaks. These high expenditures were artifacts brought by most probably the following insurance settlement policy: when annual expenditures by the facility do not reach 96% of the capitation budget, facility does not receive its full annual amount. The CD/OP benefit designated facilities might carefully contain the costs at the beginning of each financial year, and the annual expenditure might not reach 96% of the capitation budget. The only way to reach the annual expenditure target by the closing of the financial year was to intentionally raise the cost, which would explain the positive post-implementation expenditure trend. This settlement policy was designed to secure the quantity of care but brought unintended negative outcomes. These negative effects got smaller in 2011 and vanished in 2012, when the insurance programs tightened the routine checks, the designated facilities understood more clearly about the incentives embedded in the settlement system, and management and clinical practices changed accordingly. Zhuhai drew the lessons that, without carefully designed and refined settlement policies, the potential cost containment effect of provider payment reforms might not be realized.[36]

Quality of care

A successful provider payment reform should contain irrational cost escalation without compromising the quality of care. In Zhuhai, we found some positive effects on antibiotic and injectable use in the designated primary care facilities after the introduction of the CD/OP benefit with capitated provider payment: the use of injectables for general OP care and use of antibiotics and injectables for ARI patients significantly decreased and presented long term reduction effects. This result is in line with the findings of two reviews about provider payment reforms[37] and two case studies in China: the capitation payment with "pay-for-performance" system led to significant improvement of four prescription indicators in Shandong, and a reduction of approximately 15% in primary care antibiotic prescriptions in Ningxia.[38,39]

It is not clear whether any long-term effects are solely linked to the introduction of the CD/OP benefit, as other initiatives of regulating antibiotic and injectable use in OP care in 2011 and 2012[40] might also have had a positive effect. The capitated provider payment

with pay-for-performance (linking the performance with year-end liquidation) is the most important component of Zhuhai's health insurance reform. Such a combination intended to help avoiding the negative effects of prospective provider payment, so as to secure the quality of care (including quality use of medicines). More recently, pay-for-performance has gained acceptance as well in both developing countries like Rwanda and Philippines[41-43] and developed countries like UK and US.[44-46]

It is disturbing in Zhuhai that no positive effect was observed for antibiotic use in general outpatients, which may be due to unintended adverse incentives created by the financial regulations. Despite a modest reduction after the introduction of the CD/OP benefit, the 2012 levels of antibiotic and injectable use of 53% and 31% remain much higher than the target of 20% set by the Zhuhai Health Bureau in 2011[47] and internationally standards.[48] It is also

Table 6 Proportion of primary care outpatient visits with prescriptions of at least one antibiotic and injectable (2012) compared to external standards

Indicators	Proportion of primary careoutpatient visits with at least one antibiotic	Proportion of primary care outpatient visits with at least one injectable
Zhuhai common disease outpatient visits, 2012[a]	53%	31%
Zhuhai common disease outpatient visits for ARI 2012[a]	68%	42%
Target set by Zhuhai Health Bureau, 2011[b]	<20%	<20%
Urban community health centers 2008[c]	45%	NA
WHO public facilities (median), 2006[d]	50%	20%
WHO private for-profit facilities (median), 2006[d]	47%	20%
WHO private non-for-profit facilities (median), 2006[d]	45%	40%
WHO South Asia region (median), 2006[d]	50%	12%
WHO Latin American & Caribbean region (median), 2006[d]	40%	NA
WHO East Asia & Pacific region (median), 2006[d]	NA	35%
WHO public facilities for ARI low-income (median), 2006[d]	90%	NA
WHO private facilities for ARI low-income (median), 2006[d]	50%	NA

Sources:
a Zhuhai Human Resource and Social Security Bureau;
b Zhuhai Health Bureau;
c The 4th National Health Service Survey;
d The World Health Organization. Using indicators to measure country pharmaceutical situations-Fact book of WHO level I and II monitoring indicators. Geneva: WHO; 2006.

higher than the national average of 45% in urban community centers in 2008[49] (Table 6). The same the case for the studies in Shandong and Ningxia,[38,39] where, although the capitation payment with pay-for-performance improved antibiotic prescriptions, use remained high. This finding may again reflect the fact that perverse incentives on prescribing have not been removed. Besides cost-containment measures, other policies are now needed to promote scientifically sound and cost-effective prescribing. In addition, financial incentives may not be able to improve clinical practices on their own—although they might succeed in doing so if they are aligned with quality improvement goals. The effect of capitation plus pay-for-performance on medicine use was not firm and promising in Zhuhai, as specific quality of care targets (including use of medicines) were missing from the performance inspections system.

STUDY LIMITATION

To our knowledge, this is one of few studies about China in which routine health insurance claim data were systematically used to evaluate impacts of an important policy change. Interrupted time series is the strongest quasi-experimental research design for evaluating policy effects.[12,13] Yet our ability to attribute changes in utilization, expenditures, and quality of care to the implementation of the CD/OP benefit was restricted in two ways. First, the electronic insurance claims data system was part of the CD/OP benefit implementation and electronic insurance claims data prior to the CD/OP benefit were therefore not available. This prevented us from measuring the values of most outcome indicators before the CD/OP benefit was implemented. In addition, the 46 CD/OP primary care facilities were designated at different time points over the course of five years, further complicating inference based on a strong quasi-experimental design. We replaced missing pre-policy claims data with data provided by individual facilities. These data are likely less accurate as they are not used for payment purposes. For indicators with missing baseline data, we compared outcomes among CD/OP enrollees to those among the overall resident population. We acknowledge that these comparisons are less than ideal as the groups partially overlap. Yet it is reassuring that outcome indicators among the overall Zhuhai population do not show discontinuities at the time of the CD/OP benefit implementation, indicating that there may not have been competing interventions accounting for the changes we found. Finally, our measurements of costs and prescribing quality before August 2009 are based on data from four early-designated facilities only and may not be fully representative of all CD/OP designated facilities.

The lack of one consistent longitudinal source of data also highlights one of the strengths of our study, namely the use of different types of routine data collected by different actors in the system to study impacts of policy interventions. The Zhuhai Municipal Health

Insurance, the Zhuhai Health Bureau, and selected health care facilities all contributed data for this study. Their collaboration with academic partners exemplifies multi-stakeholder engagement, which is essential for studying and improving health systems over time.

CONCLUSION

The CD/OP benefit with capitated provider payment had begun to fill gaps in the basic health insurance system in Zhuhai. Payment for OP care shifted from MSAs among about half of the insured population to a pooled insurance fund for which all insured are eligible. This change greatly enhanced access to primary care for CDs of urban and rural residents and migrant workers, who benefited most because they did not have MSAs and had to pay out-of-pocket for CDs formerly. The increased access to primary care seems to have led to a reduction in expensive specialist IP services for CD/OP enrollees.

The CD/OP benefit with capitated provider payment also seems to have contained expenditures. Cost awareness in designated primary care facilities was likely raised, although some perverse financial incentives remain to be addressed. Use was somewhat reduced, but still high. Financial incentives may help to improve clinical practices only if they are aligned with quality improvement goals. Policies other than just cost-containment measures but more explicit incentives and specific quality of care targets (including use of medicines) are needed to be incorporated into the pay-for-performance system for the capitated provider payment, in order to promote scientifically sound and cost-effective care and treatment in Zhuhai.

The systematic design, implementation, and evaluation of the Zhuhai CD/OP benefit with capitated provider payment may provide a model for other insurance schemes. We hope that our careful documentation of Zhuhai's first experiences using routinely collected data from different sources will inform other systems in China as well as other relevant countries in designing and implementing basic health insurance coverage policies on the way to universal coverage.

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Chapter 6

General Discussion

The aim of this thesis is to use policy impact analysis to obtain evidence on effective health system reform policies to improve the use of medicines. To that end, the status and trends of the Chinese health system, as well as the challenges of the Chinese pharmaceutical sector, and the rationale for making an impact analysis of various components of health system reforms on medicines were analyzed. Next, effects were analyzed of various strategies to promote appropriate use of medicines. This thesis aims to answer the following research questions:

1.What are the general strengths and challenges of the Chinese pharmaceutical system?

2.What are the effects of clinical educational interventions on medicines use, with a focus on antibiotics?

3.What are the effects of various financing reforms on the use of health services and medicines within the health system reform framework?

4.What are the effects of integrated system reforms on the use of health services and medicines within the health system reform framework?

In this final chapter, the main findings are presented and discussed, followed by a review of possible policy implications for more efficient reforms towards improving the use of medicines. Some methodological challenges of pharmaceutical policy impact analysis are discussed, and areas for further research are identified.

MAIN FINDINGS

Research question 1: What are the general strengths and challenges of the Chinese pharmaceutical system?

The overall situation of the Chinese pharmaceutical system was described in Chapter 2. The Chinese pharmaceutical system has experienced a rapid development following the economic reform. Emerging issues in medicines R&D, registration, pricing, distribution and clinical use in the new market economy environment needed to be addressed with more rigorous and effective regulation policies and strategies. We found that, before the most recent wave of nationwide health system reforms starting in 2009, prescribing of medicines, especially antibiotics, was frequently inappropriate; too many medicines, especially too many antibiotics and injectables were prescribed. We also found that distorted incentives in the health systems are the key drivers of inappropriate use, and that it is critical to remove these in order to create a clear policy environment for appropriate use. We also found that the lack of an appropriate national medicines policy to align economic development with health

objectives is another obstacle towards the development of a healthy pharmaceutical system. The strengths of the Chinese pharmaceutical system are that access to essential medicines has generally been secured through universal coverage of the population with basic health insurance. The challenges are that benefit packages need to be further strengthened, and that a pro-poor perspective is needed to secure more equal access to quality care (including quality use of medicines). In addition, the "safety net" function is to be reinforced to prevent catastrophic pharmaceutical expenditures of poor families.

Research question 2: What are the effects of clinical educational interventions on medicines use with a focus on antibiotics?

Clinical educational interventions on the use of antibiotics and the effects of these interventions were analyzed in Chapter 3. Limited effects were observed for clinical educational interventions to improve the use of antibiotics: after the interventions, huge gaps remained between actual performance and internationally agreed guidelines. Our studies found that although the most strict and intensive nationwide interventions significantly reduced antibiotic use in Chinese hospitals, their use remains far from scientifically sound. Simple restriction of use did not lead to scientifically sound and cost-effective use of antibiotics. The general dislike of basic and cheaper antibiotics like penicillins and other narrow scope antibiotics seems deeply rooted.

Research question 3: What are the effects of various financing reforms measures on the use of health services and medicines within the health system reform framework?

This question was addressed in Chapter 4. The effects of the two most important financial components of the health system reform: the allocation of increased government subsidy and the reform of the medicines mark-up and provider payments were analyzed. Removing the mark-up on the sale of medicines is one approach to reverse the perverse incentive of relying on medicines sales of health facilities, in order to eliminate one important driver of inappropriate use. We found that an appropriate financial allocation with government subsidy to offset the lost medicines revenue can help to resolve the infrastructure, staffing and salary issues, and can have an important impact on the use of medicines. In Beijing, a fixed government subsidy to primary care completely delinked providers' income from medicines mark-up, as no surplus was allowed to be kept by the primary care. There was neither an incentive to generate more revenue nor one to procure medicines outside the essential medicines list. This enabled more use of essential medicines, and helped containing the rising costs of medicines. However, this approach did not create any incentive for keeping sufficient work enthusiasm and motivation. Another allocation approach kept the government subsidy in place but also allowed mark-ups of non-essential medicines. Here the perverse incentives were not totally removed, and no change in the use of medicines was observed.

Another type of financing reform concerned changes in provider payment within the basic health insurance programs. Shifting from a retrospective "fee-for-service" payment towards a prospective capitated payment removes the motivation of inappropriate use of medicines and cost inflation. We found that in Qianjiang, such a provider payment shift contained rising medicines costs without any unintended results such as increased patient referrals and hospitalizations. However, this single financial reform did not significantly change prescription behavior.

Research question 4: What are the effects of integrated system reforms on the use of health services and medicines within the health system reform framework?

Zhuhai's experience in designing the outpatient benefit package with capitated provider payment (Chapter 5) supported the concept that universal health coverage (UHC) needs to be achieved in three dimensions: the degree of population coverage, the range of service coverage and the level of financial risk protection. Our studies found that the creation of one pooled fund for universal access to a minimum primary care outpatient benefit package increased the efficiency of the participating health insurance funds. Coordinated reform policies supporting each other and creating the appropriate incentives could help to achieve UHC with a secured level of quality of care. The method of capitated payment for the contracted primary care providers raised their cost awareness, and helped to reduce the escalation of costs. But a simple prospective provider payment change alone did not secure the quality and efficiency of care. A carefully designed pay-for-performance system is needed to create the appropriate incentives, and to ensure that the payment reforms do not lead to unintended effects.

DISCUSSION OF THE MAIN FINDINGS

Universal health coverage (UHC) and healthy pharmaceutical systems

Developing appropriate national pharmaceutical policies to secure health objectives

Our findings showed that developing an appropriate national medicines policy that aims to match the economic development with the health objective is essential for the development of a healthy pharmaceutical system. The pharmaceutical policies of countries always have multiple objectives. Health is regarded as a fundamental human right by the United Nations,[1] and the goal of sustainable improvement of the standard of health is therefore at the centre of a pharmaceutical policy. High performance national pharmaceutical policies require the coordination of interrelated objectives, clarity of policy goals and objectives, awareness of policy instruments and options, and understanding of policy impacts and interactions.[2] In its practical application, conflicts between various components of the policies are common, particularly when certain aspects of pharmaceutical policies are set by various government

agencies with fractured responsibilities. This is even more so in countries with a large population and huge geographical, demographical, social and economic disparities, like India and China.[3]

Our studies found that the changing Chinese pharmaceutical policies unfortunately failed to be integrated but generated several inconsistencies. For example, pharmaceutical policies with contradictory goals have created distorted market incentives in the health systems. Our studies also found that the government intends to develop a strong local pharmaceutical industry to contribute to the economic development; that selling medicines has been used as a tool to cross-subsidize public health providers as a compensation of declined government investment; and that price caps have been regarded as a means to secure access for the poor. This combination of policies has created a vicious cycle with multiple perverse incentives. The viability of the pharmaceutical industry came to rely on "under the table" deals with health service providers, instead of appropriate returns following normal marketing exercises. Health service providers had to rely on medicines sales rather than on the quality of health care services. The availability and accessibility of life-saving essential medicines was neglected as no profit could be made with low-priced medicines. The affordability of medicines for the poor was not secured as low-priced medicines were not made available anymore. Even with continuous price caps, the financial burdens of neither the government nor the society nor individuals were relieved.

Promoting efficient use of medicines to secure financial viability

Our studies demonstrated inefficient use of medicines in China; unnecessary and incorrect use is quite common. Prescribing of medicines, especially antibiotics, is frequently inappropriate. Too many medicines, especially too many antibiotics and injectables, are prescribed. Our studies also noted that these problems have not fundamentally changed after the national health system reforms. These findings are supported by extensive other empirical studies about medicines use in China, which were internationally published three to five years after the health system reforms.[4-10] Use of medicines is one of the major drivers of quality, safety, equity, and cost of care in the health systems of low and middle-income countries (LMIC).[11] The problems of inappropriate use of medicines in China are even more serious than in many other (LMICs).[12-14] Pharmaceuticals constitute a major expenditure of the health systems, including out-of-pocket payments by the poor. The pharmaceutical system therefore has a significant role in determining the economic burden on the government, the society and individuals.[15] Medicines also constitute three of the top ten sources of waste of scarce health system resources.[16] The problem of inappropriate use of medicines therefore has been creating a huge challenge for China—a country with the world largest population but limited health resources per capita.

Following the most recent wave of the health system reforms, China claimed to the world that it achieved UHC.[17] Analysis of the progress towards UHC with selected indicators also shows positive trends.[18] According to an estimation by IMS,[19] China is expected to have the highest growth of medicines expenditure in the world, where per capita spending will grow by over 70% during 2015-2020. The subsequent efforts of China to expand access, promote inclusiveness, and advances in innovation will all have a bearing on the use of medicines. Without considering the non-compliance of clinical guidelines, which may bring additional cost due to adverse drug reactions or resistance, on the basis of over-use alone UHC in China would already not be sustainable. The experience of South Korea in implementing UHC and its dilemma of spiraling costs should be carefully considered by China.[20] The challenge for China now is to expand health services with constant attention to causes of waste and inefficiency that can be reduced through smart policies and wise decisions.[21] The sooner effective interventions are identified and implemented, the sooner the risk of financial unsustainability of UHC is reduced.

Clinical educational interventions and prescription behavior in complex health systems

Our findings have demonstrated the limited effects of clinical educational interventions before and at the early stage of the health system reforms. In our study settings, clinical educational interventions, even linked to managerial measures, were obviously not enough to counteract the deep-rooted perverse incentives. Rather than simple restriction of use, more sophisticated and comprehensive policies are needed when hospital financing is heavily dependent on medicines sales, and prescribers themselves also gain additional income from dispensing or selling medicines. In addition, the reversed proofing responsibility for medical disputes also encourages a defensive and high-prescription attitude of doctors. These powerful factors greatly influence their prescription behavior and are not fundamentally resolved through clinical educational and even managerial interventions.[22-24]

The lack of positive effects of clinical educational interventions that we studied confirmed that prescription behavior is determined by a variety of internal and external, social, economic and cultural factors. The effectiveness of interventions on prescribing depends to a large degree on the content, delivery mechanisms, intensity, context and implementation environment. Interventions on medicines use can be put into several categories, including clinical educational, managerial, financial and regulatory measures.[25,26] Effective interventions are always broad-based with multiple dimensions, adapted to a particular situation, and addressing local barriers to change. No single intervention can be recommended for all behaviors in any setting.[15,27,28,29,30] The most extensive review of experiences from developing countries concerning medicines use surveys and studies (1990–2009)[31] found that interventions undertaken to combat inappropriate use of medicines that have been of a clinical educational nature, have had a

relatively small impact and have usually not taken into account the determinants of behavior. Our studies about interventions on antibiotic use in Chinese hospitals also confirmed this. A combination of interventions, involving managerial as well as educational components appears to be more effective than a single intervention. Successful interventions on the use of medicines have to address the socio-economic and cultural factors, and adapt to specific settings with a coordinated strategy package.[15] This is particularly true in complicated health systems like our study settings in China.

Financing mechanisms and prescription behavior

Our findings about the effects of the two most important financial components of the health system reform (Chapter 4) showed the importance of financing mechanisms in changing prescription behavior. In many resource poor LMICs where health systems are not appropriately funded and regulated, economic factors can be important barriers to compliance with guidelines.[22] How health care is financed and how health care providers are paid substantially affects treatment decisions, because the financing mechanisms create different incentives for health care providers.[32] New and more sophisticated financing mechanisms have evolved with units of payment becoming broader, and prices for bundles of services set on a prospective basis.[33,34]

Allocation of government subsidy

The experience of Beijing presented in Chapter 4 confirmed that sufficient government expenditure ensures the base for promoting appropriate use of medicines.[29] Studies in other areas of China[35,36] also demonstrated that a secured government subsidy to primary care helps promoting the use of essential medicines and containing the rising trend of medicines costs. However, the input-based direct government subsidy and retrospective service-based provider payment might not create the necessary incentives to increase efficiency. Yip and her colleagues[37] also noted that the fundamental difficulty of eroded medical professional ethics has not been tackled in any of the experiments so far. Secured government funding may help to resolve the infrastructure, staffing and salary issues. However, prescription behavior will still not be fundamentally improved through increased government funding only. Avoidance of perverse financial incentives is one of the core policies to promote appropriate use of medicines.[29] As long as the perverse incentives of generating revenue and the distorted pricing system are not changed, prescribing patterns will never become optimal.

Provider payment incentives

Our study in Qianjiang presented in Chapter 4 showed that the cost containment objective was achieved through provider payment reforms. This fits with many other local health insurance provider payment reforms in China that have shifted from a passive bill payer (which

encourages the over-supply of expensive treatments) to a service "purchaser" approach, using payment methods other than fee-for-services to encourage cost-consciousness. Provider payment reforms have been mostly effective in influencing health expenditure patterns,[38] and have been implemented in both high income countries (HICs) and LMICs to contain health care costs.

Any successful provider payment reforms should contain irrational escalation of costs without compromising the quality of care. In addition to cost, many other factors must also be addressed in health care provider payment reforms. These include the unintended effects of aggregated and prospective payment methods, such as reduced service quality, reduced service, and excluding sick patients.[39-41] Evidence of cost containment through provider payment methods has been reported, but very little is known about its impact on these other dimensions, including the quality of care. More comprehensive strategies are needed to secure the quality of care when containing the cost.

Integrated system reforms and prescription behavior

Our findings about the basic health insurance reforms in Zhuhai described in chapter 5 proved that integrated system reforms of the insurance programs helped in improving the use of medicines. The impact of such reforms on prescription behavior heavily depends on the comprehensive and careful design of the supporting policies. An appropriate pay-for-performance system with specific indicators of quality of care (including quality use of medicines) is especially critical for effective prescription behavior improvement.

The important role of insurance programs

Like what we found in Zhuhai (chapter 5) the basic health insurance programs play an important role in helping improve the use of medicines. The pooled basic health insurance funds have become the key source of revenue for all levels of public health facilities in China after the achievement of UHC. In 2011, the national basic health insurance expenditure accounted over 50% of the total medical and medicines revenues of all levels of health facilities, and even reached 80%—90% in some areas.[42-44] A large amount of government funding was newly allocated to the health sector in the first three years of the national health system reform (CNY 850 billion, US$ 125 billion, exchange rate=6.8).[45] The government decided that most of this additional finance should be used to subsidize those that were not already covered by the basic health insurance programs in both urban and rural areas.[46] Increased government investment in health also led to shifting resource allocation towards performance-based government procurement (supply side) and subsidy to the vulnerable groups to pay for basic health insurance (demand side). With continued expansion of access to more comprehensive services and strengthening of benefit packages, the issue of efficient use of the insurance funds emerged. As the third party payer, the health insurance

programs must be responsible for the viability of the insurance funds, and play a more and more important role in resource allocation, creating incentives and constraints, regulation and supervision.

Our findings are in line with those of a study of Chen et. al. in primary care facilities in China,[47] which measured the changes of prescription patterns under the economic incentives created by the reform, and strongly suggests that payers need to be involved in the health care financing reform. The study found that the overall changes were not significant, two years after the implementation of the national essential medicines system reform in which health insurance programs were not comprehensively involved. It seems that the removal of a perverse economic incentive alone would not lead to improvement of health providers' prescribing patterns. The lack of payers' and providers' meaningful involvement in the reform process possibly contributed to the lack of significant change in prescribing behaviors.

Pay–for–performance based capitated provider payment

We found that in Zhuhai (Chapter 5), a combination of pay-for-performance system with the capitated budgets for primary care providers helped in raising the awareness of cost of the providers. However, inappropriate prescribing of antibiotics and injectables remained prevalent, although it partially improved. According to Gold and Felt-Lisk's recommendations of using physician payment reform to enhance health system performance,[48] broadly speaking a well-designed prospective payment system would promote safe, effective, patient-centered, timely, efficient, and equitable care. This suggests that additional and more explicit incentives to improve the quality of care (including the quality use of medicines) should be incorporated into the provider payment system. Such clear and specific quality of care indicators were missing in Zhuhai's pay-for-performance based capitated provider payment system. That may explain why Zhuhai did not fully achieve the prescription behavior change objective of the reform.

Our findings in Zhuhai (Chapter 5) also indicated that to reach appropriate financial incentives through health care provider payment reforms, designers of health insurance programs need to have the necessary managerial and technical capacity. The year-end settlement policy in Zhuhai is a good example of this. The policy was set intending to secure the quantity of services under the capitated payment system (promoting motivation), but brought an unintended side-effect of artificial cost inflation at the end of the financial year. There might be more appropriate measures to secure the quantity of service and to promote motivation rather than controlling the actual expenditure. This reflects the limited capacity of the insurance programs in creating a system of appropriate performance indicators. The question of what dimensions of performance need to be addressed is large and complex. However, with the huge capacity and experience constraints in China, especially at primary

care level, most performance indicators are only related to cost control and service volume, which have only a weak association with health outcomes. It is not yet clearly established how much of a provider's income has to be linked to quality-related performance to induce a behavioral change in treatment.[38]

Our findings about the intended and unintended effects of the financial year-end settlement policy in Zhuhai also indicated that strong incentives for some services may reduce the quality of other services. There is already some evidence in China that providers make up outcomes that give them higher performance assessment scores.[38] Maynard and his colleagues[49] argue that the international literature is not clear as to how large the incentives (rewards or penalties) must be to generate needed behavioral change and what are the opportunity costs, including the costs of good monitoring and objective data. Like our findings in Zhuhai (chapter 5) demonstrated, many primary care reforms in China claim that they tie performance to activities or quantity of services rather than objective or measurable indicators of quality. As a result, without specific targets on the quality of care, the incentives for the pay-for-performance based capitated provider payment system differ little from those of fee-for-service payment in Zhuhai. The pay-for-performance system, in order to be cost-effective, can best be applied to services for which the quality and outcome are clear and easy to measure. Clearly defined evidence-based treatment protocols can be used for performance assessment.[38]

STRENGTHS AND METHODOLOGICAL CHALLENGES

Strengths of the thesis

The set-up of this thesis follows the development of the health sector reform program in China, starting with simple and individual reforms and moving towards more complex and comprehensive reforms. As far as we know, this thesis is the first comprehensive study comprising of a series of empirical research projects about the effects of China's most recent health system reforms on medicines use. The studies cover the various components of the reforms in different stages at either central or local level. The key components of these reforms include: clinical educational interventions on use of medicines, financing reforms like removing the mark-ups on medicines, allocation of government subsidies to health care providers, shifting the health care provider payment from retrospective to prospective method, exploring pay-for performance system linking with prospective health care provider payments; and designing new benefit packages to achieve universal health coverage. This thesis tracks the pathway of the reforms in sequence, from clinical educational interventions to individual financing reforms, and to integrated system reforms with a health system approach to improve the quality of care (including medicines use). It also analyzes the complexity of medicines use problems and the necessity to address the long lasting problems in China with an integrated health system approach.

To our knowledge, the thesis also presents the first study in China in which routinely collected health system data, including insurance claims data, have been systematically collected and analysed to assess the impacts of health system reforms in China. Our careful documentation and evaluation of various reform components has very important implications for other areas of China, which are seeking to improve access to health services and financial protection through universal health coverage. The strengths of the thesis include the use of data from different sources to construct relevant policy indicators, a strong quasi-experimental design to assess change in selected indicators, and references to relevant Chinese documents to make this information accessible to non-Chinese experts.

The lack of one consistent longitudinal source of data also highlights one of the strengths of our final study of this thesis, namely the use of different types of routine data collected by different actors in the system to study impacts of policy interventions. The results present proof of concept that existing data from different sources can be used to inform health policy in China. More advanced study methodologies are now needed to better document the most effective interventions. The collaborations of all government agencies to contribute data for this study with academic partners exemplifies multi-stakeholder engagement, which is essential for studying and improving health systems over time.

Methodological challenges

Sample characteristics and selection bias

In the first study described in this thesis, the selected regions, manufacturers, health facilities and pharmacies for the survey were with secured representativeness. The reviewed prescriptions were systematically selected from a random day of the studied year. This might bring prescription selection bias due to the seasonal change, differences in patient attendance across months, weeks and working days within the same hospital. If the reviewed prescriptions were selected across the studied year, the potential bias could be reduced.

In another two early studies described in this thesis, we used a simple random sampling method to select facilities, which might not have the selected facilities adequately representative of the characteristics of scale and operation status of the health facilities. We stratified the facilities by administrative district before sampling in Beijing, which helped to attribute the above factors to some extends more adequately. The risk of potential selection bias might be higher in Qianjiang due to the constraints that reform was implemented in several stages, and there were only a small number of facilities that started the reform in the first group. These did not allow us to do any stratification of the facilities.

A later study described in this thesis collected data on antibiotics use from selected Chinese hospitals. Ideally, we would have used the existing Chinese national monitoring network data to conduct this study but these were not available. The selected hospitals are part of the 35 hospitals who firstly reported data to the national monitoring network. This may have concerned relatively advantaged settings, as the selected hospitals may have more motivated clinical pharmacists to conduct routine monitoring and audit of antibiotic use, and thus actually be better than the average of all hospitals. This implies that the problems that we noticed may still be an underestimation of the real situation.

The last study described in this thesis targeted the insured population voluntarily enrolled in a new primary care benefit in Zhuhai. There might be a potential selection bias when we compared the population enrolled to the new benefit with the overall insured and the overall resident population. As the new benefit is voluntary, there might be a potential adverse selection by patients, i.e., unhealthy population is more willing to enroll than the healthy one. Such selection bias may lead to over estimation of the primary care service utilization and cost of this population.

In addition, due to the constraints of availability of insurance claims data before the introduction of the new benefit, we had to approach to individual primary care facilities to ask for baseline data. As the primary care facilities were designated by the new benefit at different time points over the course of five years, there were only a limited number of primary care facilities set up electronic database before 2009. To obtain electronic data before 2009, we only identified four individual health facilities that could provide electronic data to replace the missing insurance claims data before the introduction of the new benefit. This may not be fully representative of all the facilities designated by the new benefit; but these were the best data available.

Quality of data and information bias

The early study in Shandong and Gansu was jointly conducted by the research team and the local health administrative and regulatory authority officials. Such collaboration facilitated in some way the willingness of manufacturers, health facilities and retail pharmacies to provide concrete data and information. To secure the interview quality, all data collectors and interviewers were trained with standardized interview tools.

In order to facilitate data collection, another two early studies presented in this thesis heavily relied on existing health administrative data in Beijing and Qianjiang. Although the Health Bureaus organized regular trainings for health facilities to conduct appropriate data collection and reporting, possible quality problems may still exist. However, these are likely to be limited in size because of the quality assessment.

The later study presented in this thesis used antibiotics data directly extracted from routine electronic databases of the selected hospitals, which greatly improved the validity of the data. Another benefit of this study is that the outcome measures of this study are mostly in line with what the national monitoring network used, and all the studied hospitals are members of this network. This enabled us to validate the extracted data through comparing what they reported to the network. In addition, to reduce the potential errors led by human factors in different hospitals, the data provided by each studied hospital were double checked by two researchers by graphing and comparing with the others over time.

The last study presented in this thesis in Zhuhai used multiple sources of health system data which have been routinely collected. As our major data source, the health insurance claims data is a large high quality whole population database, which leads to sufficient power for precise estimation and measurement, and reduced the potential errors by human factors in the process of data extraction and prescription.

Causality, confounding control and study design

Unlike testing the efficacy of a medicinal product, investigating the efficacy of a particular policy intervention is complex, due to the variety of possible causes of any observed trend. Randomized double-blind experiments are the gold standard by which effectiveness is measured in clinical disciplines, but they can be impossible to implement when it comes to social policy assessment.[50] Controlled before-and-after studies and interrupted time-series studies are two types of quasi-experimental designs, in addition to randomized experiments, to improve the quality of information for decision-makers.[51] These are scientific study designs for situations where no control group is possible (e.g. measuring the impact of a national policy), as in our studies. In such cases analyses of interrupted time series are the strongest design. This adds to the validity of our findings.

Among the four key policy impact analysis studies as described in this thesis, the study designs were improved progressively, starting from early simple "before and after comparison" with non-perfect control group, moving to the strongest quasi-experimental design to evaluate the longitudinal effects of policy interventions. This gradual improvement may be interpreted as a beneficial effect of a continuous quality monitoring.

In our early studies in Qianjiang and Beijing, with the only available annual average data and reforms implemented in stages, the assessment was restricted to a rough trend analysis rather than a longitudinal study. The comparison among different groups of facilities which started the reform in different stages helped to control the confounding policies effects to a certain extent. The annual average data for Qianjiang was influenced by the effect of

reforms in facilities which started to reform in different times during the year. Although the contributors were small comparing with overall Qianjiang and could be neglected, the average data of overall Qianjiang was still not a perfect controller.

The later studies presented in this thesis (antibiotics use in hospitals and Zhuhai) used a fully longitudinal design. These studies are among the first in China using different sources of routine administrative data. A segmented regression analyses of interrupted time series data was used to measure changes in the level and trend overtime, and to conduct cross-sectional comparisons against external standards. This adds to the validity of our findings

Another advantage of our studies presented in this thesis (antibiotic use in hospitals and Zhuhai) is that we conducted a chronological policy review around the studied time period. This kept tracks of all relevant policies that were introduced or implemented at the same time as our targeted policy interventions. It also helped in explaining the largely varying results that might be the effect of underlying factors. The interactions between various policies, and their respective contribution to the observed changes of measurement outcomes were considered as possible hidden contributing factors.

IMPLICATIONS

Implications for policy and practice

Appropriate institutionalization

Our studies of the impact of interventions on improving the use of medicines at the early stage of the health system reform found that simple and isolated interventions had very limited effects, whereas we found some positive effects of some more extended interventions programs. This implies the need of multi-disciplinary and multi-faceted approach. As shown in Chapter 3, the Swedish Strategic Program against Antibiotic Resistance (STRAMA) is a good example of such an approach. A multi-disciplinary and multi-faceted approach is needed to develop, implement and evaluate interventions to promote appropriate use of medicines.

Our finding that a multifaceted and multidisciplinary approach is relatively successful also implies a need for a relatively strong coordination, given the very strong financial and societal interests of this issue. To achieve this, a dedicated body to coordinate the policies, strategies, activities between the various stakeholders is needed at both national and regional levels. The new body may involve as many stakeholders as possible, including government, health professionals, academia, pharmaceutical industry, consumer groups and non-governmental organizations.[29] We recommend that the decentralized, segmented government agencies related to medicines use (including various medicines use and

resistance monitoring networks) work towards better integration and coordination, sharing resources and information.

Sufficient public funding

Like many other studies,[35,36,38,52] our study (chapter 4) has shown that secured government funding has supported the implementation of the "medicines zero mark-up policy", by relieving the financial burden of the community health centers in Beijing. This funding has removed the perverse incentive of relying on medicines sales to generate revenue. This implies that an appropriate level of public financing for sufficient and competent health personnel is critical to improving the use of medicines. This is the precondition for any effective program. We also found that additional incentives are needed to address the issues of eroded professional ethics and motivation.

Financial incentives

Our findings have demonstrated that perverse financial incentives are one of the most important factors leading to the inappropriate use of medicines and rising costs in China; the distorted pricing system for medicines and medical care is at the root of the problem. This implies that to fundamentally change the inappropriate prescription behaviors, perverse financial incentives must be removed where possible. This may be reached through reforms in the pricing system, shifting from the current "cost-plus" government price control system to a system of value-based pricing of medicines, raising the price of medical services, and increasing the salary scale of health care professionals.

We also found that insurance programs as the third-party-payer, using provider payment as a financial leverage, were able to raise cost awareness of the primary care providers in Zhuhai (Chapter 5). Economic factors are important barriers to guideline compliance in resource-poor settings,[22] and financing mechanisms create different incentives for health care providers.[32] How health care is financed and how health care providers are paid therefore substantially affects their treatment decisions. This implies that it may be necessary to involve and strengthen the role of the basic health insurance programs in relevant health care financing reforms.

Our findings showed that a simple shift from retrospective to prospective payment did not fundamentally change the prescription behaviors in Qianjiang. It also did not work with a weak "pay-for-performance" system in Zhuhai, as both of them paid little attention to the quality use of medicines. This implied that provider payments used to create an appropriate financial incentive for cost-effective quality care must be linked with a pay-for-performance system based on specific quality indicators, rather than on a simple cost containment indicator.

Our finding that the year-end settlement policy of Zhuhai insurance programs brought an undesirable side-effect of artificial cost inflation at the end of the financial year implies that it is urgently needed that the budget management capacity in some specific issues be increased at all levels of governments and insurance programs. These issues include the actuarial valuation to rate the pre-payment, and cresting a comprehensive pay-for-performance indicator systems based on treatment guidelines and process outcome of specific major conditions, service volume, patients' satisfaction, etc. In addition to capacity building, the result of our studies in Zhuhai also imply that, in order to include quality indicators into the pay-for-performance based provider payment system, the insurance agencies will need to work more closely together with the health administrative agencies in developing and implementing the clinical pathways for disease diagnosis and treatment (including medicines treatment), and use these as a base for the quality of care driven pay-for-performance system. Linking prescription audit and other quality of care control measures with health facility accreditation may be a good approach.

Evidence–based clinical guidelines

Evidence-based standard clinical guidelines are critical tools in promoting the appropriate use of medicines.[29] Our studies described in Chapters 3 found that one of the main factors that the antibiotic clinical use guideline was not well complied was the guideline itself - it was not operational for some issues, and there were contradictions between different guidelines. This implies that institutionalization of a mechanism for developing evidence-based standard clinical guidelines, making them acceptable to multiple levels of professionals, and keeping them operational can contribute to the improvement of medicines use.

Integrated health system approach

Our findings about the impact of various interventions on improving use of medicines showed that clinical educational interventions hardly changed the prescription behaviors, and confirmed that isolated reform initiatives have limited effect. This may imply that effective interventions on medicines use have to address the key determinants of prescribing behaviors. More strategic approach carrying a health system perspective is needed. Demands from either the patients or the health professionals need to be considered. This includes mobilization of technical and public resources to educate both the health professionals and the public on prudent use of antibiotics and other medicines; promoting monitoring and evaluation of medicines use and relevant policies with appropriate methodologies to better inform medicines policy making; building harmonized relationship between different stakeholders in the health system, etc. Our studies presented in Chapter 3 found that doctors are risk-averse for high-risk patients, leading to a defensive use of antibiotics. This is one important reason for over-use of antibiotics and inappropriate antibiotic prophylaxis.

This implies that there may be a need to adjust the legislation of placing the responsibility of proof on doctors in medical disputes about unexpected infections, in order to enable a better patient-doctor relationship and reduce the unnecessary use of antibiotics.

Information and data sharing

Our studies in Zhuhai as described in Chapter 5 have used multiple existing databases, with each data source providing information of additional value. This implies that existing data from different sources (including the insurance claim system, health administrative reporting system and specific medicines use monitoring systems) can be used to inform policy making. Our studies in Beijing, Qianjiang and Zhuhai all used routine electronic data shared by health administrative authorities and local insurance programs. Without their support, our studies would have needed much greater financial means and other resources to facilitate the data collection. A route may be to make annual reports of various monitoring networks available to the public. Making raw data for academic research may be beneficial to improving the health system.

Implications for future research

Regular assessment of the health system reform and medicines use

Our studies have targeted several key components of the health system reforms in China over a limited time period only, and have showed several components to be effective but other ones to be ineffective. Such practices provide evidence of the most effective reform initiatives, which can better inform the health system reform decision makers and promote evidence-based policy adjustments. A mechanism of regularly gathering and evaluation of new health system reforms is to be created at both the national and local level. A platform is to be set up for posting these reform policies and the impacts assessment results on line and make it publicly accessible. This can serve as a strong tool of evidence-based health policy-making through the comprehensive and rigorous analysis of the dynamics of health care system reforms.

Our studies in Zhuhai as presented in Chapter 5 have found that specific quality indicators about prescription behaviors were missing in Zhuhai's pay-for-performance system for the capitated provider payment. This may explain the unacceptable high use of antibiotics and injectables after the reform, even though the cost awareness of health care providers was raised. Although the insurance programs conducted regular inspections to the affiliated health facilities, they did not include a comprehensive indicator system to check the quality of care. This implies that, a set of standardized quality of care (including appropriate prescriptions) indicators is to be developed for insurance programs to be used for routine management and supervision. It would be ideal if these indicators could satisfy the needs of both quality control and cost containment. National targets are also necessarily to be set for

these core indicators, to direct all stakeholders towards a gradual improvement of the use of medicines. A real-time database can be used to identify problems in general prescribing and quality of care, and to design appropriate interventions and to measure the impact of those interventions. Like it is being done in Oman and in many high incoming countries, a secondary evaluation of these indicators is needed for targeting interventions for managing the rational use of medicines.[53] These secondary evaluations can by conducted by age, by level of care, by geographic area, by category and diagnosis. The routine analysis results of these indicators can also be used by either insurance programs or health authorities as a reference for various administrative and management purposes.

Further in–depth incentive studies

Our studies have targeted two key components of the financing reforms: government subsidy allocation and capitated provider payment. In addition, our impact analysis of these financing reforms on the quality of care has only focused on limited traditional medicines use indicators, like the proportion of essential medicines prescribed, the proportion of prescriptions with antibiotics and injectables, etc. In reality, various other financial incentives are implemented as well, and this holds too for the quality of care. There are only few experiments in China with re-aligning incentives for health care providers on the basis of these studies. Preliminary evidence suggests a potential to produce cost savings, but evidence of their effect on quality and health outcome is limited. This implies that a systematic review and impact analysis of the incentives for quality care in China is critically needed. These incentives can target either the supply side (health care facility and health professionals) or the demand side (patients) in different settings. Research is needed to study how to optimize these incentives, in order to correct for the current financial distortions in the health system. These incentives include appropriate pricing policies for medicines and medical services, and new approaches to government subsidies, health insurance reimbursement policies, health insurance payment methods to health care providers, taxes and tariffs.

Mixed approach with quantitative and qualitative methods

The studies presented in this thesis have included extensive interviews with different stakeholders and key informants. The obtained information was used in the discussion to elaborate, illustrate and clarify the research findings and some contradictions from the quantitative analysis. This component of quantitative research might be further enriched if it were combined with more formal qualitative methods, which can contribute to better understanding of the underlying reasons of any variation in outcomes. Mixed methods in social science research are defined as a technique that combines quantitative and qualitative research. It helps to reduce researcher bias, thereby increasing the credibility of the findings. There has been an increasing acceptance of the concept of mixed methodology research

techniques, methods, approaches, concepts or language into a single study.[54,55] Such mixed methods are needed for future impact analysis studies, in order to expand the breadth and range of quantitative research, and to help understand not only whether and to what extent, but also why certain changes took place.

ATC/DDD system for comparative drug utilization study

Our findings about the comparison of antibiotic use in Chinese and Swedish hospitals (Chapter 3) have found that the Chinese medicines classification system is only partially in line with the global Anatomic Therapeutic Chemical (ATC) system, so our comparison could only target limited ATC categories of antibiotics. This implies there is a need for China to adopt the international ATC classification system, in order to be able to improve prescription monitoring systems. International comparative drug utilization studies can help countries to exchange and share information, and to use the experiences of other countries in their own efforts to improve the use of medicines. The Anatomic Therapeutic Chemical (ATC) / Defined Daily Dose (ATC/DDD) system is recommended by the World Health Organization as a tool for drug utilization research in order to improve quality use of medicines. One component of this is the presentation and comparison of drug consumption statistics at international and other levels. Though providing much new information, our studies on medicines use still only mapped a general situation of medicines use, and lacked more detailed drug utilization studies for specific diseases. This implies there is a need to collect and analyze disaggregated data in terms of gender, age and geographic area, targeting specific diseases, in order to facilitate international collaboration and to allow for better international comparisons.

CONCLUSION

China's pledge to provide affordable, equitable access to quality basic health care for all its citizens is laudable, and its reforms in the medicines area may serve as a useful model for other countries.[56] Now that universal access to basic health services and essential medicines has largely been achieved, future challenges include stronger risk protection of individuals, and appropriate incentives for better efficiency and quality of care.

Removing remaining perverse incentives (e.g. those where hospitals and doctors rely on the sale of medicines to compensate for low salaries of health workers or lack of other institutional revenue) is the pre-condition for any successful and sustainable reform in the medicines area in the Chinese health care systems. Creating appropriate incentives through carefully designed and comprehensive health financing reforms in both the supply side (health care provider financing) and the demand side (reimbursement to patients) is now one of the top priorities for China to improve the efficiency and cost-effectiveness of health care. It is now necessary to design an effective bundled payment system with mixed

approaches, as well as a comprehensive pay-for-performance indicator system with specific quality of care targets.

Before any reform decisions are made, it is necessary to at least conduct a mapping and quantification of the current state of the problem. Indicator-based assessments followed by more detailed studies on individual medicines or specific diseases and on the availability/affordability of essential medicines, are also needed.

Strong quasi-experimental studies with time-series data are extremely useful to monitor progress towards defined targets, and can also serve as a baseline for newly-planned interventions. From these quantitative data, decision makers will be able to understand accurately their major problems, design appropriate reforms and monitor their impact.

Our thesis has given proof of concept that routinely collected data from different sources can be used to construct relevant policy indicators. Combining routine health system and health insurance reimbursement data can show us the impact of policy changes and can contribute to the evaluation and improvement of health system reform policies in China.

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Summary
Samenvatting
小结

Medicines are major contributors to health when used appropriately, and they waste resources and endanger health when overused or used incorrectly. Perverse incentives in the health systems can lead to seriously inappropriate use of medicines, which is especially serious in settings with scarce health resources. Innovative and integrated system reforms to promote a more evidence-based use of medicines are required to remove the perverse incentives. The aim of this thesis was to obtain evidence on effective policies to improve the use of medicines by analyzing the impact of the health system reform policies in China. This evidence can hopefully be used by the Chinese government and by other relevant countries when developing or adjusting their health system reform policies to improve use of medicines.

In **Chapter 1**, we describe the status and trends of the Chinese health system. We analyze the challenges of the Chinese pharmaceutical system, and elaborate the rationale for making an impact analysis of various components of health system reform policies on medicines. The following research questions were formulated:

1.What are the general strengths and challenges of the Chinese pharmaceutical system?

2.What are the effects of clinical educational interventions on medicines use, with a focus on antibiotics?

3.What are the effects of various financing reforms on the use of health services and medicines within the health system reform framework?

4.What are the effects of integrated system reforms on the use of health services and medicines within the health system reform framework?

Chapter 2 sets the scene of the overall situation of pharmaceuticals and medicines use in China. First we examined the main problems in the whole supply chain of pharmaceuticals, from registration, production, distribution, to utilization and administration, and analyzed the main socio-economic and institutional factors associated with these key problems. We found that the pharmaceutical sector of China experienced a rapid development following the economic reform of the country. Emerging issues of research and development of new medicines, registration, pricing, distribution and clinical use in the new market economy environment must be addressed with more rigorous and effective regulation policies and strategies. It is critical to remove any perverse incentives in the systems to create a clear policy environment. It is also essential for develop an appropriate National Medicines Policy, to balance economic development and health objectives. We also measured the availability and use of essential medicines in two provinces of China, just at the time of the most recent

wave of health system reform in 2009. The results can therefore be regarded as a baseline measurement for the reform. We found that manufacturers, retail pharmacies and hospital pharmacies paid limited attention to the national essential medicines list in their decisions to manufacture, purchase, and stock essential medicines; prescribing of essential medicines was frequently inappropriate. These results could be used to develop strategies to improve affordable access to essential medicines under the current health system reform.

Chapter 3 describes clinical educational interventions on antibiotic use and analyzes the effects of these interventions. We first focused on antibiotic prophylaxis in Chinese hospitals, reporting on a systematic review of 82 intervention studies on antibiotic prophylaxis in clean or clean-contaminated surgery in Chinese hospitals from 2000 to 2012. The review found that all but one study claimed effectiveness of interventions; that limited effects were observed for antibiotic prophylaxis in non-indicated clean surgery; and that huge gaps remained between the international agreed guidelines and the claimed best performance after the interventions. We also found that a simple measurement of the outcome indicators as an average for the performance of pre– and post-intervention groups failed to distinguish the real intervention effect from confounding factors, and failed to adjust for any underlying trends. More advanced study methodologies are needed to better document the most effective interventions.

We next studied the impact of the 2011 nationwide intensive interventions on the use of antibiotics. Our study analyzes changes in the patterns of antibiotic use in Chinese hospitals, and compares these with Chinese national targets and with antibiotic use in Swedish hospitals. We found that the 2011 interventions significantly reduced antibiotic use in Chinese hospitals. The proportion of prescriptions with antibiotics dropped 4.7% ($p=0.03$), and the proportion of medical records with antibiotics dropped 7.3% ($p=0.04$). However, the proportions of prescriptions and medical records with antibiotics in Chinese hospitals in 2012 (10% and 50% respectively) are still much higher than Swedish hospitals (1.1% in DDDs for outpatients and 34% in number of patients for inpatients). Inpatient consumption pressure in Chinese hospitals also significantly dropped to 473 DDD/1,000 inpatient days in 2012 compared to 910 in 2008 and 588 in Swedish hospitals in 2012. Antibiotics are being used less frequently in Chinese hospitals, but broad spectrum antibiotics are still preferred, and gaps are still huge. From the evidence of this study, we cannot tell whether the changes in China result in less inappropriate antibiotic use, so further studies are needed.

Chapter 4 includes two studies on the effects of the "medicines zero mark-up policy", which aimed to remove the reliance of providers on medicines sales, and “provider payment reform” which intended to shift the resource exhausted retrospective payment to cost sensitive prospective payment. These two studies target the most important financial

components of the health system reforms, with the aim to remove the perverse incentives for medicines overuse and cost escalation, and to create a positive incentive for cost-effective use and cost awareness. The studies both focus on primary care where the two reform components were initiated, one in urban area, and the other in a rural area. The first study reports on the effect of implementing three different health care financing mechanisms in Beijing community health facilities in parallel with introduction of the "medicines zero mark-up policy". This study analyzes the cost containment effect and its effect on the operation of community health facilities. We found that a fixed subsidy (FS) is more effective than an income-linked subsidy (IS) and government purchasing services (GPS) in containing cost. GPS causes lower willingness to use “zero mark-up” medicines. Medical professionals under the FS have lower work enthusiasm than under the other two types of financing mechanisms.

We also report on the effect of shifting the provider payment from a fee-for-service system to capitation payment in Qianjiang, a less developed county in western China. The new rural cooperative medical scheme of Qianjiang regarded the provider payment as a tool to contain costs and to change prescription behaviors. We found that the growth rate of cost was contained at the beginning of each stage of reform but that the effect disappeared thereafter. Except for a significant increase of essential medicines prescription in health centers, prescription behaviors were not significantly improved. No significant change in referral rate was observed but the hospitalization rate shifted from an upward trend to a downward trend after the reform. The monthly income and outpatient revenue continuously increased. We concluded that the capitated payment reform in Qianjiang achieved its cost containment objective without unintended results, but failed to achieve its objective to improve prescription behavior. More comprehensive combined policies are needed.

Chapter 5 records the initiatives of one special economic development (Zhuhai) area in developing integrated health system policies to improve medicines use. First we document local experiences in designing and improving the basic health insurance system from the dimensions of population coverage, service coverage and financial risk protection. This paper describes chronologically the development of Zhuhai’s basic health insurance system. It analyzes the background and the key components of the common disease outpatient benefit package, and makes a comparison with outpatient benefit packages of other areas of China and four neighboring countries. It also summarizes the strengths and weakness of the package, and lists the remaining research questions for future studies. We present the first study in China in which routine data from various sources were systematically collected and analysed to assess the effect of a local health insurance reform programme. Longitudinal data from the health insurance organizations, the health administrative bureau, and primary care facilities were used to assess trajectories in outpatient visits, inpatient admissions, cost

per common disease outpatient visit, and prescribing indicators over time. The study found that the number of total outpatient visit at 46 primary care facilities (designated by the CD/OP benefit as of July 2012) increased 46,895 visits/month (p=0.004, 95% CI: 15,795~77,994); the average number of CD/OP visits reached 1.84/year/enrollee in 2012.. Monthly inpatient admissions dropped from 6.4 (2009) to 4.3 (2012) per 1,000 enrollee; the average total cost per CD/OP visit was reduced CNY 15.40 (p=0.16); injectable use was reduced 7.4% (p=0.03) but antibiotic use was not improved. We conclude that Zhuhai's new CD/OP benefit with capitated provider payment has expanded access to primary care, which may have led to a reduction in expensive specialist inpatient services for CD/OP benefit enrollees. Cost awareness was probably raised, and rapidly growing expenditures were contained. Although a small improvement was seen, inappropriate prescribing of antibiotics and injectables remained prevalent. We conclude that more explicit incentives and specific quality of care targets must be incorporated into the pay-for-performance system of capitated provider payment, in order to promote scientifically sound and cost-effective care and treatment. The methodology of the study also highlights that existing data from different sources can be used to inform health policy in China.

In **Chapter 6** a summary of the main findings are followed by a review of possible policy implications for more efficient reforms towards improving medicines use. The results of this thesis show that universal access to basic health-services and essential medicines has largely been achieved in China. Future challenges include stronger risk protection of individuals, and appropriate incentives for better efficiency and quality of care. Removing perverse incentives in the health systems is the pre-condition for any successful and sustainable reform in the medicines area. Creating appropriate incentives through carefully designed and comprehensive health financing reforms in both the supply side and the demand side is now one of the top tasks for China to improve the efficiency and cost-effectiveness of health care. Designing an effective bundled payment system with mixed approaches, as well as a comprehensive pay-for-performance indicator system with specific quality of care targets is needed. Before any reform decisions are made, it is at least necessarily to conduct mapping and quantification of the current state of the problem with appropriate methods. An indicator-based assessment followed by more detailed studies on individual medicines or specific diseases, and the availability/affordability of essential medicines is needed. Our thesis has given proof of concept that routinely collected data from different sources can be used to construct relevant policy indicators.

Geneesmiddelen kunnen een belangrijke bijdrage leveren aan de gezondheid - mits zij goed worden gebruikt. Zo niet, dan verspillen zij geld en brengen zij de gezondheid in gevaar. Verkeerde prikkels in het gezondheidssysteem kunnen leiden tot incorrect geneesmiddelengebruik; dit is vooral een groot probleem in situaties met beperkte financiële middelen. Innovatieve en geïntegreerde systeemhervormingen, waarvan objectief is vastgesteld is dat zij werken, zijn nodig om zulke prikkels te verwijderen. Het doel van dit proefschrift is om bewijsmateriaal te verzamelen over effectief geneesmiddelenbeleid, door middel van een analyse van het effect van recente gezondheidshervormingen in China. Dit bewijsmateriaal kan hopelijk gebruikt worden door de regeringen van China en van andere landen, wanneer zij hun beleid willen aanpassen om geneesmiddelengebruik te verbeteren.

In **Hoofdstuk 1** beschrijven wij de huidige toestand en trends in het Chinese gezondheidssysteem, en vatten wij onze redenen samen om het effect te meten van de verschillende onderdelen van de gezondheidshervormingen. De volgende onderzoeksvragen zijn geformuleerd:

1. Wat zijn de sterke kanten en de huidige uitdagingen van het Chinese geneesmiddelen systeem?

2. Wat zijn de effecten van klinisch-educatieve programma's op het gebruik van geneesmiddelen, met name op het gebruik van antibiotica?

3. Wat zijn de effecten van de verschillende hervormingen van het financieringssysteem op het gebruik van gezondheidszorg en geneesmiddelen?

4. Wat zijn de effecten van geïntegreerde systeemveranderingen op het gebruik van gezondheidszorg en geneesmiddelen?

Hoofdstuk 2 beschrijft de algemene situatie van geneesmiddelen en geneesmiddelengebruik in China. Eerst beschrijven wij algemene problemen in de voorziening van geneesmiddelen, van het moment van registratie, productie, distributie tot voorschrijven en toedienen, en analyseren wij de socio-economische en institutionele factoren die met deze problemen samenhangen. Wij vonden dat de geneesmiddelensector in China een snelle ontwikkeling doormaakte tijdens de economische hervormingen in het land. Nieuwe problemen op het gebied van geneesmiddelenonderzoek en ontwikkeling, registratie, prijsstelling, distributie en klinisch gebruik in de nieuwe marktomgeving moeten nu krachtiger worden aangepakt met sterke strategieën en effectieve regelgeving. Het is heel belangrijk dat verkeerde prikkels in het system worden weggenomen. Het is essentieel dat er een effectief geneesmiddelenbeleid wordt geformuleerd, waarin de juiste balans wordt gevonden tussen economische ontwikkeling en gezondheidsdoelen. Wij hebben ook de beschikbaarheid en het gebruik van geneesmiddelen

gemeten in twee provincies van China, precies ten tijde van de eerste gezondheidshervormingen in 2009. Deze resultaten kunnen daarom beschouwd worden als een basismeting voor de hervormingen. We vonden dat de fabrikanten en apothekers weinig aandacht besteedden aan de nationale lijst van essentiële geneesmiddelen bij hun beslissingen om essentiële geneesmiddelen te produceren of in te kopen; en voorschrijfgedrag was vaak onjuist. Deze uitkomsten zouden gebruikt kunnen worden om strategieën te ontwikkelen om de toegankelijkheid tot goedkope geneesmiddelen te bevorderen onder de huidige hervormingen.

Hoofdstuk 3 beschrijft klinisch-educatieve programma's over het gebruik van antibiotica, en analyseert het effect van deze interventies. Eerst besteden wij aandacht aan antibiotische profylaxe in Chinese ziekenhuizen. We geven een overzicht van 82 interventiestudies over antibiotische profylaxis in schone of schoon-geïnfecteerde chirurgische operaties in Chinese ziekenhuizen tussen 2000 en 2012. De review vond dat in alle studies behalve één een positief effect werd geclaimd; dat er slechts een gering effect werd gevonden op het niveau van antibiotische profylaxe in niet-geïndiceerde schone operaties; en dat er een groot verschil bleef bestaan tussen de internationale richtlijnen en de als "best resultaat" geclaimde eindresultaten. Wij vonden ook dat een simpele uitkomst indicator voor het gemiddelde antibiotica gebruik voor en na de interventies er niet in slaagde om het werkelijke effect van de interventie te scheiden van dat van verstorende factoren, en ook niet kon corrigeren voor onderliggende trends. Er zijn meer geavanceerde methoden nodig om de meest effectieve interventies te documenteren.

Daarna bestuderen wij het effect van intensieve nationale interventies in 2011. Wij analyseerden de veranderingen in het gebruik van antibiotica in Chinese ziekenhuizen, en vergeleken dit met de nationale doelen en met het gebruik van antibiotica in ziekenhuizen in Zweden. Wij vonden dat deze interventies een significant effect hebben gehad op het gebruik van antibiotica in Chinese ziekenhuizen. Het percentage recepten met één of meer antibiotica werd 4.7% lager (p=0.03); het percentage opnames met één of meer antibiotica nam ook af, met 7.3% (p=0.04). Toch bleven deze percentages in Chinese ziekenhuizen in 2012 veel hoger dan in Zweedse ziekenhuizen (1.1% bij Defined Daly Doses voor ambulante patiënten en 34% bij aantallen opgenomen patiënten). Gebruik bij opgenomen patiënten in Chinese ziekenhuizen viel significant terug tot 473 DDD/1,000 patiëntdagen in 2012, vergeleken met 910 in 2008 (588 in Zweedse ziekenhuizen in 2012). Antibiotica worden nu minder vaak gebruikt in Chinese ziekenhuizen, maar er bestaat wel veel voorkeur voor breedspectrum antibiotica. Uit deze studies kunnen wij wel opmaken dat er minder antibiotica gebruikt worden, maar niet of de interventies ook hebben geleid tot beter antibiotica gebruik.

Chapter 4 presenteert twee studies over het effect van het "nul-marge op geneesmiddelen verkoop" beleid, wat erop gericht was om de economische afhankelijkheid van medicijnverkoop weg te nemen bij ziekenhuizen; en van het "betaal de leverancier van zorg" ("fee-for-service")

beleid, wat erop gericht was om achterafbetaling van geleverde zorg te vervangen door een vooruitbetaald bedrag ("capitation fee"). Deze twee studies analyseerden de twee meest belangrijke elementen van de nieuwe hervormingen, met als doel om de verkeerde prikkels weg te nemen die hadden geleid tot overconsumptie van geneesmiddelen en escalatie van kosten, en een nieuwe prikkel te scheppen voor kosteneffectiviteit en kostenbewustzijn. Beide studies waren gericht op de eerstelijnszorg, één studie in een stedelijk gebied en de andere op het platteland. De eerste studie beschrijft het effect van drie verschillende financieringsmechanismen in eerstelijnszorg in Beijing, tegelijkertijd met het "nul-marge voor geneesmiddelenverkoop" beleid. De studie onderzocht het effect op kostenbeheersing en op het werk in de gezondheidscentra. Wij vonden dat een vaste subsidie (Fixed Subsidy, FS) effectiever is in kostenbeheersing dan een inkomensafhankelijke subsidy (IS) en een inkoop system (government purchasing system, GPS). GPS leidt tot minder gebruik van "zero mark-up" geneesmiddelen. Het FS systeem demotiveerde gezondheidswerkers meer dan de andere twee systemen.

We beschrijven ook een studie naar het effect van het veranderen van betaling voor geleverde zorg ("fee-for-service") naar een systeem van vaste betaling per patiënt per jaar ("capitation fee") in Qianjiang, een minder ontwikkelde provincie in West China. Het nieuwe coöperatieve gezondheidssysteem in die provincie beschouwde deze betalingen als een instrument om de kosten te beheersen en voorschrijfgedrag te veranderen. Wij vonden dat de kostenstijging inderdaad tijdelijk beperkt werd in het begin van de hervorming, maar dat het effect na enige tijd verdween. Er was wel een langdurige stijging in het gebruik van essentiële geneesmiddelen in gezondheidscentra. Er waren geen verbeteringen in het voorschrijfgedrag of het percentage verwijzingen naar het ziekenhuis, maar de aantallen ziekenhuis opnames namen wel af. Het maandelijkse inkomen in de kliniek door de behandeling van ambulante patiënten nam toe. Wij concludeerden dat het capitatie systeem zijn doel van kostenbeheersing had bereikt, en zonder ongewenste bijwerkingen; maar dat het doel van beter voorschijfgedrag niet bereikt was. Totaaloplossingen zijn nodig.

Hoofdstuk 5 beschrijft de initiatieven in een economische ontwikkeling speciaal gebied (Zhuhai), waarbij geïntegreerde oplossingen om medicijngebruik te verbeteren werden geïntroduceerd. Eerst beschrijven wij de lokale ervaringen met het ontwerpen en verbeteren van simpele gezondheidsverzekeringssystemen vanuit het perspectief van de dekkingsgraad van de bevolking, het service aanbod en de bescherming tegen financieel risico. Deze studie beschrijft in chronologische volgorde de ontwikkeling van Zhuhai's basale verzekeringssysteem. Het analyseert de achtergrond en de belangrijkste componenten van het pakket voor ambulante zorg, en vergelijkt dit met de pakketten in andere gebieden van China en in vier buurlanden. Het vat ook de voor- en nadelen samen, en presenteert een lijst van onderwerpen voor toekomstige studies. Daarna presenteren wij de eerste studie in China waarbij routinematig verzamelde gegevens van verschillende bronnen op systematische manier werden verzameld

en gecombineerd om de effecten te meten van het nieuwe verzekeringsprogramma. Longitudinale data van verzekeringsmaatschappijen, de gezondheidsadministratie en eerstelijns gezondheidscentra weren gebruikt om het verloop te schetsen van patiënten aantallen, opnames, kosten per eerstelijnsconsult, en voorschrijfgedrag. De studie vond dat het aantal ambulante consulten in 46 eerstelijnscentra (die per Juli 2012 officieel door de verzekering waren erkend) verhoogde 46.895 bezoeken per maand (p = 0,004, 95% CI: 15.795 ~ 77.994); het gemiddelde aantal CD / OP bezoeken bereikte 1.84 per jaar per verzekerde in 2012. De maandelijkse ziekenhuisopnames daalde van 6.4 (2009) tot 4.3 (2012) per 1000 verzekerden; de mediane kosten per bezoek en het gebruik van injecties waren beiden verminderd, maar niet het gebruik van antibiotica. Wij concluderen dat Zhuhai's nieuwe verzekeringssysteem met capitatie systeem de toegankelijkheid tot eerstelijnszorg heeft verbeterd, wat geleid kan hebben tot een vermindering in aantallen dure specialistenopnames voor de verzekerden. Het kostenbewustzijn was waarschijnlijk verhoogd, en snel stijgende kosten werden beteugeld. Hoewel er een kleine verbetering zichtbaar was, bleef onjuist voorschrijfgedrag van antibiotica en injecties bestaan. Wij concluderen dat meer expliciete prikkels en duidelijke doelstellingen voor de kwaliteit van de zorg toegevoegd moeten worden aan het capitatie systeem, ten einde wetenschappelijk juist en economische efficiënt geneesmiddelengebruik te bevorderen. De studiemethode laat ook zien dat het mogelijk is in China om bestaande data te gebruiken om beleidsmakers te informeren.

In **Hoofdstuk 6** wordt een samenvatting van de voornaamste bevindingen gevolgd door een beschouwing van de mogelijke beleidsimplicaties. De resultaten van dit proefschrift laten zien dat universele toegankelijkheid tot basiszorg vrijwel volledig is bereikt in China. Toekomstige uitdagingen zijn het vergroten van de bescherming tegen persoonlijke financiële risico's, en het vinden van de juiste prikkels voor meer efficiëntie en kwaliteit van de zorg. Het verwijderen van verkeerde financiële prikkels in het gezondheidssysteem is een absolute voorwaarde voor de duurzame voorziening van geneesmiddelen. Zorgvuldig ontworpen allesomvattende hervormingen van zowel vraag- als aanbodzijde moeten nu hoge prioriteit krijgen om de efficiëntie en kosteneffectiviteit van de gezondheidszorg te waarborgen. Centrale financiering moet gecombineerd worden met een systeem van indicatoren en doelstellingen om betalingen te baseren op de kwaliteit van de geleverde zorg. Voordat hervormingen ingevoerd worden moet er in ieder geval een adequate basismeting worden uitgevoerd om de beginsituatie vast te leggen. Een eerste studie gebaseerd op indicatoren moet dan gevolgd worden door meer gedetailleerde studies van specifieke geneesmiddelen of ziektes en van de beschikbaarheid, prijs en toegankelijkheid van essentiële geneesmiddelen. Dit proefschrift heeft het bewijs geleverd dat routinematig verzamelde verzekeringsgegevens van verschillende bronnen gebruikt kunnen worden om bruikbare beleidsindicatoren aan te leveren.

药品使用得当可以促进健康，过渡使用和使用不当会浪费资源和危害健康。卫生体制中的负面机制会导致不合理用药，这种现象在卫生资源匮乏的环境中尤其严重。以促进循证用药为目标的、创新和整合的改革要求必须破除卫生体制中的负面机制。本论文的目标是通过分析中国医疗卫生体制改革政策的效果，获得有效促进合理用药政策的证据。希望这些证据对中国政府和其他相关国家制定或调整其卫生体制改革中促进合理用药的政策有所帮助。

第一章描述了中国卫生体制的现状和趋势。我们分析了中国药品领域面临的挑战，阐述了针对卫生体制改革中用药相关政策进行政策效果评价的理由。形成了以下若干研究课题：

1. 中国药品领域的特点和面临的挑战是什么？
2. 基于临床和教育式的药品（侧重于抗生素）使用干预措施效果如何？
3. 医改框架下，各类筹资改革对卫生服务和药品使用的影响效果如何？
4. 医改框架下，整合的、系统的改革对卫生服务和药品使用的影响效果如何？

第二章描述了中国药品领域的概况和药品使用基本情况。首先，我们考察了从注册、生产、流通、使用到管理的药品供应全过程存在的问题，分析了与这些问题相关的重要的社会、经济和制度性影响因素。我们发现，中国实行经济改革后，药品领域经历了一个快速发展阶段。新的市场经济环境下涌现出了涉及新药研发、注册、定价、流通和临床使用等一系列问题，必须通过更有活力和更有效的监管政策和策略解决这些问题。破除卫生体制中的负面机制，创造一个“清洁”的政策环境十分重要。制定平衡经济发展和健康目标的国家药物政策也十分关键。我们还调查了两省份在中国最近一轮医改刚刚开始时（2009 年）基本药物可及性和使用情况。结果可作为医改评价的基线情况。我们发现，国家基本药物目录对药品生产企业、零售药店和医院药房的生产、采购和储存决策影响甚微，基本药物使用不合理现象普遍存在。将这些结果用于当前医改，可帮助制定促进基本药物经济可及性的政策。

第三章描述了基于临床和教育式抗生素使用干预措施，并对干预效果进行了评价。我们首先侧重中国医院预防性使用抗生素问题，报告了一项系统性评价研究。该系统评价针对 2000 年 –2012 年 82 项中国医院清洁手术和清洁 – 污染手术预防性使用抗生素干预研究。该研究发现，除一项干预研究外，所有研究都宣称干预是有效的；对清洁手术无指症使用预防性抗生素的干预效果有限；干预后情况与国际认可的指南要求相比，仍存在巨大差距。我们发现，简单地测量和比较干预前后效果指标的平均值不能区分实际干预效果和混杂因素的影响，也无法调整任何潜在趋势。需要更先进的研

究方法来更好地记录最有效的促进合理用药的干预措施。

我们接下来研究了 2011 年全国抗生素整治活动对促进抗生素合理使用的效果。我们的研究分析了中国医院抗生素使用模式的变化，并与国家目标和瑞典医院抗生素使用情况进行了比较。我们发现，2011 年全国抗生素整治活动显著降低了中国医院抗生素的使用量。含抗生素的门诊处方比例下降了 4.7% (p=0.03)，含抗生素的住院病例比例下降了 7.3% (p=0.04)。但是，中国医院 2012 年门诊处方和住院病例含抗生素的比例（分别为 10% 和 50%）比瑞典医院（门诊 1.1% 以 DDDs 为单位，住院 34% 以人天为单位）仍高出很多。中国医院住院抗生素消耗量从 910 DDD/1,000 人天（2008）显著降低到了 473 DDD/1,000 人天（2012）。瑞典医院 2012 年的住院抗生素消耗量为 588 DDD/1,000 人天。中国医院抗生素使用量减少了，但仍广泛使用广谱抗生素，差距仍然巨大。此研究获得的证据还不足说明 2011 年全国抗生素整治活动后抗生素使用更合理了，仍需要进一步研究。

第四章包含两项研究，一项是关于旨在破除医疗服务收入依赖药品销售的筹资模式－“药品零差率”；另一项是关于旨在改变资源耗尽型的后付制为预付制的医疗服务支付改革。这两项研究均锁定了医改的重要内容之一－筹资改革，旨在破除导致药品过渡使用和费用不合理快速增长的负面机制，建立促进具有成本效益的药品使用和提高费用意识的新机制。两项研究均聚焦在帅先进行上述改革的基层医疗机构，一项在城市，另一项在农村。第一项研究报告了北京市社区卫生服务机构落实“药品零差率”政策的同时，实行三种不同政府补贴模式的效果。这项研究分析了上述政策的控制医药费用的效果和对社区卫生服务机构运行的影响。我们发现，固定经费补偿模式比经费与收入挂钩的模式和政府购买服务模式获得了更好的控制医药费用的效果。政府购买服务模式降低了使用“零差率”药品的意愿。固定经费模式相比其他两种模式降低了医务人员的工作热情。

我们还报告了中国西部偏远地区黔江从按项目付费到按人头付费的医疗服务支付改革的效果。黔江的新型农村合作医疗将医疗服务支付改革作为控制医药费用和改变处方行为的政策工具。我们发现，医药费用的快速增长在改革的初期得到了控制，但效果不持续。除乡镇卫生院的基本药物使用率显著增加外，处方行为并未显著改变。改革后住院率从缓慢上升趋势变为缓慢下降趋势，但无显著变化。医务人员月均收入和门诊营业收入持续增加。我们得到的结论是，黔江的按人头付费改革达到了控制医药费用的目标，但未达到改变处方行为的目标，没有发现意外结果。要达到改变处方行为的目标，需要更完善的综合性政策。

第五章记录了中国一个经济发展特区（珠海）制定整合的卫生体制改革政策，促进合理用药的努力。首先，我们从人口覆盖、服务覆盖和完善财务风险防范三个维度记录了其设计和完善基本医疗保险制度的历程。这篇文章按时间顺序详述了珠海建立基本医疗保险制度的全过程，分析了普通疾病门诊统筹政策及背景，比较了珠海和中国其他地区以及中国的四个邻国门诊福利包的异同。文章分析了各地区门诊福利包的优劣，提出了需要进一步深入研究才能解决的问题。这是中国首个利用不同来源和系统采集的常规数据，分析和评价地方医疗保险制度改革效果的研究。研究利用医疗保险的纵向数据、卫生行政管理数据和基层医疗机构的机构数据评价了门诊服务利用、住院率、次均费用和处方指标等随时间变化的轨迹。研究发现，46家定点基层医疗机构（定点截至2012年7月）的门诊总诊次显著增加了46,895次/月(p=0.004, 95% CI: 15,795~77,994)；2012年，年均普通疾病门诊统筹诊次达到了1.84次/签约人；住院率从2009年的6.4/月/1,000 签约人降到了2012年的4.3/月/1,000签约人；普通疾病门诊统筹次均费用减少了15.40元(p=0.16)；注射用药减少了7.4% (p=0.03)；抗生素使用没有改进。我们得出的结论是，珠海普通疾病门诊统筹政策及配套的医疗服务支付方式改革提高了基层医疗的可及性，减少了签约人对高费用的专科医疗和住院服务的利用。费用意识提高了，快速增长的费用得到了控制。处方行为虽然有一些改进，但抗生素和注射药物不合理使用问题依然存在。我们得出的另一结论是，以绩效为基础的按人头付费必须融入促进提高医疗质量的激励机制和具体的医疗质量（包括合理用药）指标，才能促进科学、合理的和更具成本效益的医疗。该研究的方法提示，中国现有的不同来源的数据可以服务于卫生决策。

第六章总结了上述研究的主要发现，为旨在促进合理用药的、更有效的改革提出了可能的政策建议。此论文的研究结果表明，中国基本实现了全民获得基本医疗和基本药物。未来的主要挑战是进一步加强个人大病经济风险防范，建立促进高效和高质量医疗的适当激励机制。破除卫生体制中的负面机制是药品领域任何成功和可持续改革的前提。通过精心设计包括供、需双方的卫生筹资体系的全面改革，建立制适当的激励机制，是中国政府当前提高医疗效率、促进更具成本效益医疗的重要任务之一。需要设计混合型的一揽子支付体系，并建立一套包含具体医疗质量目标的绩效考评体系作为支付依据。在任何改革之前，都需要利用适当的方法对现状进行评估。在以指标为基础的评价之后，需要更深入的针对个体药物或个别疾病的研究，调查基本药物的可及性。我们的论文证明，来源不同的常规数据可以用于构建相关政策指标。

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About the author

Jing Sun is a pharmacist trained in public health and international health policy. She graduated from the School of Pharmacy of Peking University and the London School of Economics, with the majors of pharmaceutical chemistry and international health policy.

Jing Sun has more than 20 years work experiences in medicines areas, including lab, national regulatory authority, international organization and research institute. This renders her extensive experiences in pharmaceutical science, project management and research. Since 2004, she has been involved in providing technical support to the Chinese government in the pharmaceutical area, and contributed to China's national health system reform, especially the pharmaceutical sector reform.

As the Pharmaceutical Policy Theme Group leader of China Core Group of the International Network Rational Use of Drug (INRUD), Jing Sun has been working actively in promoting access to and rational use of medicines, and establishing National Medicines Policy in China. She also plays a role of co-country leader of BRICS Medicines Alliance, working actively in strengthening the range, depth, and quality of work on medicines access and use in collaboration with partners from BRICS countries.

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